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# *Precision*

Of the many types of anesthesia, spinal procedures are the most exacting in their requirements. Because of its pharmacological precision, NEOcaine has demonstrated its fitness for spinal anesthesia over a thirty-year period of clinical use.

In practice, NEOcaine is (1) *always sterile,* (2) *virtually flash-soluble in cerebrospinal fluid,* (3) *stable to epinephrine,* (4) *rapidly and completely absorbed without irritation* and (5) *of low toxicity in anesthetic concentrations.*

ADMINISTRATION: Employ 1 mg. of NEOcaine per pound of body weight, up to 150 mg. Dissolve crystals with spinal fluid led into the ampoule. Inject slowly with optional barbotage, using a 22 gauge needle. Contraindicated in gastrointestinal perforation, obstruction, peritonitis, severe hypotension, cerebrospinal or dorsal skin disease. Drug idiosyncrasy is rare.

SUPPLIED: Ampoules of 50, 80, 100, 120, 150, 200, 300 mg. of pure procaine hydrochloride. Boxes of 10. For continuous spinal anesthesia, ampoules of 500 mg., individually boxed.
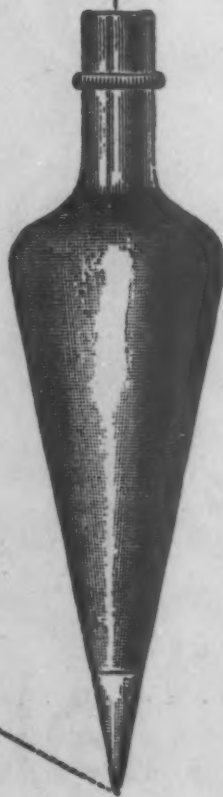
*Neocaine*
1917 1947

## MANAGEMENT OF COLOSTOMIES PERFORMED FOR WAR INJURIES

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THE PURPOSE of this communication is to report the experience with 67 colostomy cases in an Army hospital in England, and to draw a parallel between this experience and the trend of colon surgery in civilian practice.

Closure of colostomies in war casualties presented many difficulties not encountered in civilian practice. First among these were the patients with multiple injuries. Such injuries frequently produced superimposed infections, concurrent sepsis, impairment of vital organs, and general debility, all of which made the definitive surgery more hazardous. Secondly, the initial surgery was performed by surgeons in the forward area under difficult conditions so that the exact construction of the colostomy was often not clear to those who had to do the subsequent reparative work.

### PRIMARY SURGERY

The primary operative procedure recommended in injuries to the colon was simple exteriorization through muscle-splitting incisions along the course of the colon, except in wounds of the rectosigmoid and the rectum where proximal loop-colostomy was recommended if the wound in the bowel could be closed. If not, complete diversion of the fecal stream was to be practiced. In general, these procedures best served the necessity for immediate exclusion of the injured segment from the peritoneal cavity and for the control of contamination by the pathogenic bacteria present in the bowel. In addition, these patients received parenteral penicillin and sulfa drugs (the latter both intraperitoneally and parenterally) during the postoperative course.

Even under the somewhat primitive conditions at the front, physiologic balance in these patients was carefully restored preoperatively by the admin-

istration of whole blood, plasma, and solutions of electrolytes. This phase represents one of the great advances of war surgery. Much of the credit for mortality reduction in combat-wounded must go to the forward surgeons who not only did skillful emergency surgery but also practiced energetic resuscitation.

### ANALYSIS OF MATERIAL

Material for this presentation was collected over approximately one year in a General Hospital in England. It is summarized in Tables I and II.

#### TABLE I
##### SITE OF INJURY IN 67 COLOSTOMY CASES

| | |
|---|---|
| Right colon | 13 |
| Transverse colon | 9 |
| Left colon | 15 |
| Rectosigmoid | 37 |
| Rectum | 7 |
| Total | 81 |

It is quite apparent that at least 14 patients had multiple wounds since there was a total of 81 injuries in only 67 colostomy cases.

#### TABLE II
##### SITE OF COLOSTOMY IN 67 CASES

| | |
|---|---|
| Cecum | 11 |
| Right colon | 6 |
| Transverse colon | 9 |
| Left colon | 13 |
| Sigmoid colon | 30 |
| Total | 69 |

An additional decompressive cecostomy was performed in two patients who had left-sided colostomies, hence the apparent discrepancy in total number.

The types of colostomy seen at this hospital are classified in Table III.

#### TABLE III
##### TYPE OF COLOSTOMY

| | |
|---|---|
| Cecostomy | 11 |
| Double-barrel (Mikulicz) | 42 |
| Loop | 16 |
| Total | 69 |

Table III shows that there were 11 cecostomies and 58 colostomies. Of the 11 cecostomies, five were complete exteriorizations and seven were catheter cecostomies. The exteriorizations were largely unnecessary. In all but one case of extensive damage and loss of the cecal wall, a catheter cecostomy after closure of the perforations would have been preferable.

The double-barrel colostomy and the loop-colostomy were the types most frequently seen. Too often they failed of the intended purpose or created troublesome complications for the following reasons:

(1) Muscle-splitting incisions containing bowel were placed too near the costal margins or the iliac crests, with the production of osteomyelitis of these structures.

(2) Colostomies were placed too near coexisting cystostomies.

(3) The colon was brought out through the exploratory incision and was not adequately mobilized. This led to retraction of the stoma, infection of the abdominal wall, intraperitoneal sepsis, sinus formation, and wound dehiscence. The error was particularly prevalent in colostomies of the transverse colon. In retrospect, it would have been better in many cases to make a transverse exploratory incision at a lower level and to bring out the damaged segment through an intramuscular incision higher up. If a vertical incision is to be used, the colonic loops should be brought out well laterally, for instance with the proximal loop on one side and the distal loop on the other. The important thing is to keep the colostomy away from the exploratory incision. In civilian surgery this is not always necessary, or even desirable, because proper precautions can be taken, but in war surgery the instructions were to remove the clamps immediately so that no colostomy could become obstructed through neglect. With feces spilling over a fresh wound, infection is inevitable.

(4) Occasionally, missile wounds of entry or exit were used for the colostomy. Such wounds invariably became infected and developed spreading cellulitis, adding to the difficulties of eventual reconstruction.

(5) In a few cases the loops of the Mikulicz colostomy had not been sufficiently mobilized so that the spur was too short, the bowel retracted, and the loops became rotated and partially obstructed. Blind crushing of such spurs is a particularly hazardous procedure because it cannot be determined beforehand whether there is interposition of mesentery or adherence of loops of small intestine.

(6) Loop-colostomies were occasionally found with edema and necrosis underneath because of glass rods or heavy rubber tubing. Such devices are no substitute for adequate mobilization of the loop. In other cases the incision through which the bowel had been brought out was too small, with resultant constriction and partial dysfunction of the stoma.

(7) Some loop-colostomies were found to have excessively large openings, often in the transverse axis of the bowel rather than in the longitudinal axis. Small wounds of the bowel that are incapable of being exteriorized (such as in the rectosigmoid) will heal satisfactorily if primary suture approximates the edges accurately and without tension. Under such circumstances the proximal decompressive colostomy with a small anti-mesenteric opening can be closed later by simple extraperitoneal suture.

(8) In wounds of the rectum and extensive wounds of the rectosigmoid with associated injury to the bladder, the urethra, and the bony pelvis, complete diversion of the fecal stream must be accomplished. Often the double-barrel colostomy did not do this, so that a revision had to be done later, with transverse section of the bowel and separation of the stomata.

(9) Drainage of the retroperitoneal and the pelvic space was not always adequate or it had been improperly established through the missile tract. Sepsis in these spaces is especially intractable and debilitating.

## RECONSTRUCTIVE SURGERY

The type of colostomy closure will be seen in Table IV:

TABLE IV

TYPE OF COLOSTOMY CLOSURE

| | |
|---|---|
| Spur crushing......................................................... | 27 |
| Spur crushing, with decompressive cecostomy.............................. | 2 |
| End-to-end anastomosis................................................ | 17 |
| Simple inversion closure of loop stomata.................................. | 9 |
| Spontaneous closure.................................................... | 5 |
| End-to-side anastomosis, with resection of cecum........................... | 1 |
| Colostomy not closed:................................................. | 8 |
|     Because of rectal wounds......................................... 4 | |
|     Because of recto-urinary fistulae.................................... 2 | |
|     Because of rectal wounds with osteomyelitis of the ischium......... 1 | |
|     Because of rectal wounds with osteomyelitis of the ilium........... 1 | |
| Total............................................................. | 69 |

In general, these patients were considered candidates for reconstructive surgery when they were in physiologic balance and when the wound infection was under control.

In the restoration of physiologic balance the important criteria are hypoproteinemia and secondary anemia. Both should be corrected before surgery is undertaken.

In the treatment of the wound infection, the establishment of proper drainage and the application of carbamide were considered great time-savers. Carbamide is a strong lytic agent for devitalized tissues without noticeable effect on the physiologic processes of wound healing. It also deodorizes the discharges by the removal of the feeding ground of putrefactive organisms. Before surgery was undertaken, the wound was rendered at least macroscopically clean and the patient afebrile.

Following is a brief summary of the preoperative, the operative, and the postoperative routine:

*Preoperative.*—(1) Proper preparation of the patient with blood and plasma, high-vitamin low-residue diet, parenteral feeding, and supplementary vitamins.

(2) Roentgenologic, sigmoidoscopic, and digital examination of the stoma, the colon, and the rectum.

(3) Low-residue diet and 2 Gm. of sulfaguanadine every four hours day and night for five days before operation. Sulfasuxidine and sulfathalidine were not available when this work was done.

(4) Irrigations of both loops of the stoma the night before operation and again just before operation.

*Operative.*—(1) Spinal anesthesia was used in all cases. With the patient anesthetized, the area of the colostomy was cleaned with soap and water and

the usual skin preparation carried out. Into each stoma a gauze tampon on a silk thread was inserted.

(2) The incision encircled the stoma and included all scar tissue. The bowel loops were dissected free from the surrounding structures, including the peritoneum. The peritoneal cavity was walled-off by warm saline packs. The edges of the colonic stoma were freed from the rim of skin and scar tissue and the everted cuff of bowel was completely mobilized. Adhesions walling-off the peritoneal cavity were disturbed as little as possible. With careful preservation of the mesenteric blood supply, an open or closed anastomosis was then carried out, depending on which was the easier. Gauze tampons were removed before suturing started. The initial suture was oo chromic catgut, continuous; the final suture was fine cotton, interrupted. After removal of the celiotomy packs, the sutured bowel was then restored to the peritoneal cavity. In cases with an adequate spur or simple loop-colostomy, extraperitoneal closure was performed in the routine manner.

(3) Crystalline sulfanilamide, 10 Gm., was introduced into the wound and the adjacent peritoneal cavity.

(4) Wound closure was by through-and-through interrupted stainless steel wire sutures.

(5) The wound was drained by a small wick of rubber tissue down to the peritoneum or to the fascial aponeurosis.

*Postoperative.*—(1) Levin tube when necessary for gastric and intestinal decompression.

(2) Penicillin and sulfadiazine for the first 72 hours. The sulfadiazine was given by vein during the first 48 hours, when the patient was unable to take fluids by mouth.

(3) Intravenous fluids, plasma, and blood transfusion as indicated.

(4) Nothing by mouth for 48 hours, followed by gradually increasing diet.

(5) Removal of the superficial drain after 48 hours and of the wire sutures on the 12th day.

(6) Roentgenologic studies after three weeks.

### RESULTS OF COLOSTOMY CLOSURES

Table V records the results of 69 colostomy closures. There was no evidence of postoperative peritonitis in any of these cases, and there were no deaths. The complications were as listed. Otherwise all wounds healed *per primam,* and the patients were discharged as cured.

TABLE V

RESULTS OF COLOSTOMY CLOSURE

| | |
|---|---|
| Satisfactory | 68 |
|     Fecal fistula, with spontaneous closure....5 | |
|     Roentgenographic evidence of narrowed bowel lumen....7 | |
|     Abdominal wall infection....5 | |
| Unsatisfactory | 1 |
| Total | 69 |

In five cases a fecal fistula developed which lasted for several days and closed spontaneously, without further trouble.

In seven patients, postoperative roentgenologic studies revealed a narrowing of the bowel lumen at the site of the anastomosis. These patients were all asymptomatic and gave no evidence of clinical obstruction. Six of these had



FIG. 1.—Colostomy brought out through major celiotomy incision resulting in wound infection, scarring and weakness of the abdominal wall following closure.

been closed by crushing, and one by end-to-end anastomosis. Because the roentgenologic examination was made only four weeks after the operation, it is quite possible that reëxamination at a later date will show resolution of the narrowing.

Five patients developed superficial infection of the abdominal wall, mostly because of the omission of drainage. Simple drainage of the abdominal wall effected cures in all these patients in a short time.

One patient was evacuated to the Zone of Interior with a persistent fecal fistula. End-to-end anastomosis had been performed in this case, probably under tension and in the presence of an extraperitoneal abscess.

All of these patients were either rehabilitated at a convalescent hospital or returned to the Zone of Interior for final disposition.

COMMENT.—The important observation in this series of cases was that the patients who had their colostomies closed by end-to-end anastomosis suffered less morbidity and had a shorter convalescence than those who were treated by the spur-crushing technic. In our patients, at any rate, end-to-end



FIG. 2.—Edema of colostomy stomata due to the presence of a glass rod beneath the openings over a prolonged period.

anastomosis of the colon proved to be a safe procedure without any evidence of the once-dreaded peritonitis.

This observation has a direct bearing on peace-time surgery. Primary anastomosis of the colon is being practiced more and more. Coller and Vaughan,[1] for instance, report very gratifying results, and their conclusions are fully substantiated by our observations. The only difference is that Coller and his associates adopted the technic as a primary procedure, whereas in our patients it was a secondary procedure the advantages of which were gradually realized.

What has made colonic anastomosis relatively safe in recent years? Probably a variety of factors.

Modern chemotherapy must certainly be considered in this connection. In our patients, both penicillin and sulfa drugs were used, and it is our impression that they were of distinct value. The beneficial effect of penicillin on peritonitis has recently been stressed again by Crile.[2] As to the sulfa drugs in the preparation of the colon for surgery, we had to use sulfaguanidine



FIG. 3.—Colostomy placed in shall-fragment wound of entry. Abdominal wall infection was associated with a persistent purulent discharged from an infected sinus tract. A stab wound incision was made to allow free and dependent drainage of the infected sinus tract.

because sulfasuxidine and sulfathalidine were not available to us. This was unfortunate, because Poth[3] has recently reported that these newer drugs are greatly superior to sulfaguanidine in their effect on the bacterial flora of the colon.

More important, perhaps, than chemotherapy is operative technic. There are two errors to be especially avoided: an anastomosis under tension; and an anastomosis with a compromised blood supply. In our opinion, these factors were more decisive than whether the open or the closed technic was used.

Theoretically, the closed technic might be said to predispose to the formation of a diaphragm, at least if the inverting sutures are too far away from the clamp, but it is interesting to note in this series that of the seven patients in whom postoperative roentgenologic examination showed some narrowing at the site of anastomosis, six had had their colostomies closed by crushing and only one by direct suture. It seems, then, that if a careful technic is used there is little to be feared in this respect.

Lastly, the treatment of the general condition receives much more emphasis now than formerly and it is here that the greatest advances have been made. Practically all patients need blood, protein, and vitamin therapy before they are ready for surgery. Once this has been attended to, it is surprising to see how quickly they overcome their infections and how well their wounds heal.

But regardless of whether it is because of better bacteriostatic drugs, better operative technic, or better understanding of the physiologic processes, the conclusion is the same: In operations on the colon bacterial contamination is no longer the catastrophe that made surgeons formerly resort to devious procedures. With proper precautions the colon can be made as safe for direct anastomosis as the other parts of the gastro-intestinal tract. It is one of the contributions of war surgery to have underscored that fact.

<div align="center">REFERENCES</div>

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# MULTIPLE POLYPOSIS OF THE COLON WITH MALIGNANT CHANGE INVOLVING COLON AND APPENDIX

## CASE REPORT

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ALTHOUGH examples of multiple polyposis of the colon are not rare and carcinomatous change often occurs in connection with them, involvement of the appendix is almost unheard of. The case to be reported here, presents all of these features.

**Case Report.**—The patient, a female, age 35, was admitted to the Surgical Service of the New York Hospital complaining of painful and bloody prolapse of the rectum. Approximately four years prior to admission she became aware of the protrusion of a "small, soft, smooth growth" whenever she strained at defecation. At first, this was readily reduced spontaneously, but after several months it became necessary to practise manual reduction, which was accompanied by great discomfort. After a year's time the mass protruded four to five inches and seemed softer and more spongy than it had previously, bleeding continuously while it was prolapsed. One year ago, while seven months pregnant, the patient began to suffer from tenesmus and had 10 to 12 bowel movements daily. Each descent of the mass was accompanied by the loss of half a cupful of blood and an equal amount of mucus. After the delivery of her child, she felt weak and tired, and was found to have lost about 25 pounds in weight. She delayed applying for admission to the hospital for some time because of domestic and financial difficulties.

Her familial and past history were without any bearing on her present condition. She had always been frail; had rheumatic fever at the age of 18, and at 21 had a thyroidectomy performed for hyperplastic goiter. She had had five pregnancies and four normal deliveries. After her third pregnancy she suffered from a moderate cystocele and rectocele and from moderate prolapse of the cervix. Four years ago the cervix was amputated and the vaginal weakness repaired. Her last pregnancy was complicated by phlebitis of the right lower extremity which left it the site of a persistent but moderate elephantiasis.

*Physical Examination.*—The patient was a pale, thin, "worn-out" woman who appeared 15 years older than her stated age. Aside from the elephantiasis, just mentioned, and the presence of moderate clubbing of the fingers which had been present for about 18 months, nothing of note was discovered on physical examination beyond those findings about to be described in connection with the rectum.

The tone of the external sphincter was notably reduced and four to five fingers could readily be introduced into the rectum, which was filled with soft, friable polypi that bled freely. Upon straining, a segment of the rectal wall 18 to 20 cm. in length was protruded. The snout-like protrusion, which apparently comprised all the layers of the organ, was covered with innumerable small polypi of a bright red color (Fig. 1). Both the extrusion and replacement of this mass caused intense pain, and 150–200 cc. of blood were discharged into the gauze dressing. After the mass had been replaced, the patient usually was quite exhausted.

*Laboratory Data.*—On admission, the hemoglobin was down to 8 Gm., the erythrocytes to 3,100,000; the leukocytes were 7,500, with 76 per cent of polymorphonuclears,

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and the serum proteins were 5 Gm. per cent. Otherwise no significant findings were noted. The barium enema was not entirely satisfactory, but polyposis of the rectum and sigmoid was demonstrated and partially substantiated by proctoscopy. Roentgenography demonstrated a single polypus in the splenic flexure and many large polypi were noted in the hepatic flexure and its vicinity.

*Course.*—The patient was treated by supportive measures; but in spite of a diet rich in vitamins, proteins and calories together with many transfusions of whole blood and infusions of amino-acids, her serum proteins had dropped in three weeks to 4.8 Gm. per cent, the hemoglobin had increased only to 10 Gm. and the erythrocytes to 4,100,000.



Fig. 1.—With the patient in the knee-chest position, after straining, a segment of the rectal wall, 18–20 cm. in length, protruded. The snout-like protrusion, which apparently comprised all the layers of the organ, was covered with innumerable small polypi of a bright red color.

On her 23rd hospital day, a loop-transverse colostomy was performed in the left hypochondrium and after the stoma was completed, the rectum was occluded by means of a pyramidal dressing. Moderate ascites was noted at this time. By the 30th hospital day her serum proteins had begun to increase and were 5.8 Gm. per cent.

On the 48th hospital day a polypus was excised from the splenic flexure, and biopsies were taken from those in the hepatic flexure through a sigmoidoscope introduced into the stoma of the colostomy. The last were reported as "adenoma malignum." The serum proteins had risen to 6.3 Gm. per cent, and the hemoglobin to 12.0 Gm.; the erythrocytes were 4,200,000.

*First Major Operation.*—In view of the patient's notable improvement in physical condition, a right hemicolectomy and ileotransverse colostomy were carried out on the

71st hospital day, an aseptic anastomosis being performed between the end of the ileum and the side of the transverse colon within 10 cm. of the open colostomy. No ascites was present. On palpation, the sigmoid contained polypi in the first 4 cm. above the peritoneal reflexion.

*Pathologic Examination.—Gross.*—The specimen removed at this operation consisted of 7 cm. of terminal ileum which opened into the ascending colon through a normal ileocecal valve, and of 37 cm. of ascending colon. Attached to the cecum was an enormous appendix of fusiform shape, which measured 14 cm. in length and about 4 cm. in general diameter. It had the proportions of a gallbladder rather than an appendix. Through the
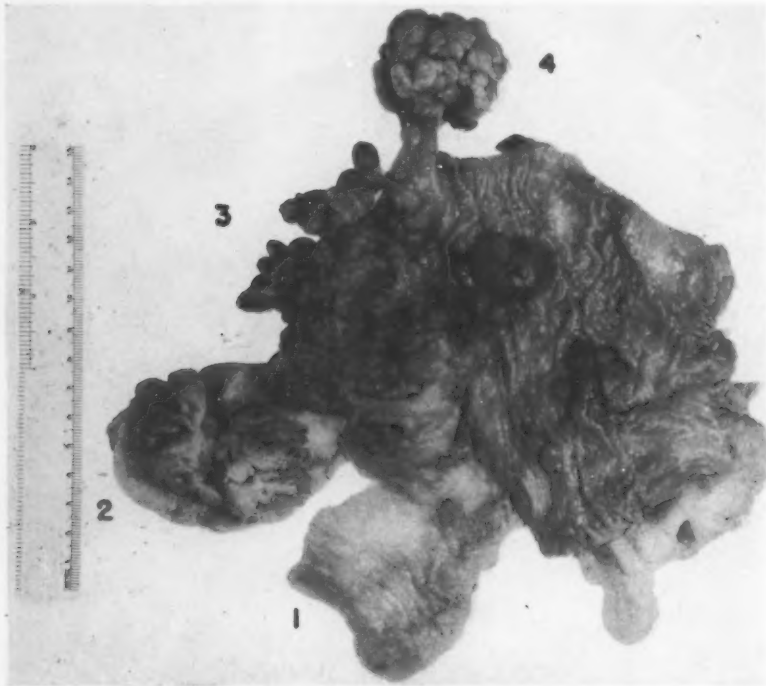


FIG. 2.—This photograph represents the cecum, appendix and part of the ascending colon. (1) Stump of the ileum. (2) Greatly enlarged and tumorous appendix. (3) Mass of polypi in the cecum, with a lighter annular area at the center, which represents the cecal carcinoma. (4) The largest of the malignant adenomas. Note the occasional smaller polypi in the ascending colon (right).

walls of the colon and appendix one could feel boggy masses of neoplastic tissue, but there was no infiltration of the parietes and the appearance of the external surface of the viscera was not noticeably disarranged.

Upon opening the specimen it was found that the entire ascending colon and cecum were covered, on their internal surface, by innumerable polypi of all sizes and shapes. Many of them had long pedicles, sometimes 4 cm. in length, others were sessile, or relatively so. The heads of these polypi were mostly red, papillary and berry-like, and many of them were obviously of the type known as "adenoma malignum." Nested in the fundus of the cecum and surrounding the ostium of the appendix there was a mass of much firmer, grayer, fungating neoplastic tissue that was obviously malignant in nature.

Following the lumen of the appendix through the ostium it was found that there

was an uninvolved zone of normal-looking appendiceal mucosa lining the constricted neck
of the organ. Distal to this the appendix was dilated into a fusiform sac, with a circum-
ference of 7 cm. at its widest point. Growing from the mucosa was a papillary tumor
made up of innumerable coarse papillae, like those of a coxcomb; they arose from a
linear pedicle 3 cm., or more, in length, about 8 mm. in width and running longitudinally
along the wall of the lumen in its middle third. The tumor projected fully 2 cm. into the
lumen from its linear origin on the mucosa. It was soft, light grayish-brown and
entirely unique in its appearance.

It is to be noted that there was no gross evidence of any physical connection between
the cecal and the appendiceal tumors. (See Figure 2, gross specimen.)

*Microscopic Examination.*—Sections from the cecal growth showed it to be a very
malignant and rapidly growing carcinoma that was definitely invasive. Sections from
representative adenomas in the ascending colon showed the usual appearance of adenoma
malignum. Those taken from the appendiceal growth (Fig. 3) revealed it to be similar
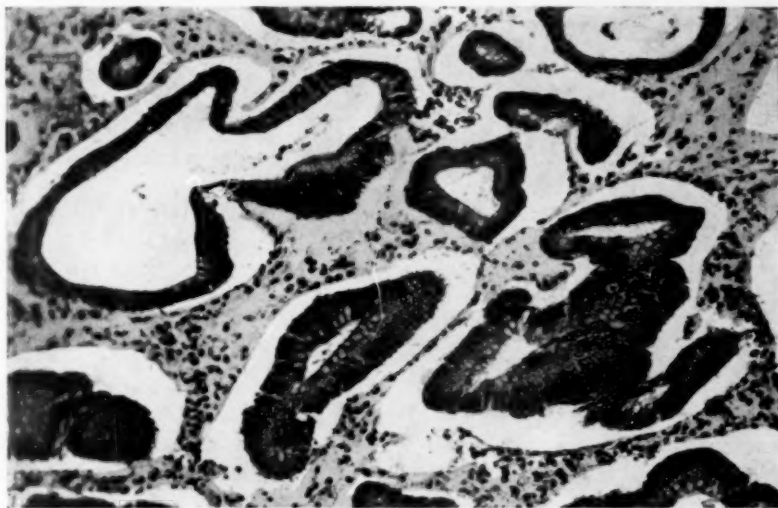


Fig. 3.—A field from the appendiceal carcinoma showing no close
similarity to that from the cecal tumor. It resembles "adenoma malignum"
of the lower intestinal tract and is fairly well-differentiated. (x 140)

in every respect to the malignant adenomas in the ascending colon. It was not a frank
adenocarcinoma like the tumor in the cecum (Fig. 4) and obviously was quite independent
of it. It presented one unusual microscopic characteristic—its stroma was extremely rich
in lymphoid tissue, possibly, to be interpreted as a result of the normally far more
abundant lymphoid tissue in the appendix.

*Second Major Operation.*—On her 80th hospital day the patient was subjected to a
perineal resection of the polypus-bearing portion of her rectosigmoid, according to the
method of Heuer. This operation has not formally been described. Briefly, the procedure
is as follows: An incision is made around the anus at the mucocutaneous junction. The
sphincter and muscle is carefully isolated and divided in the midline posteriorly. An inci-
sion is then made in the midline raphe beginning at the posterior border of the anus and
carried backward to the junction of the coccyx and the sacrum. The incision is carried into
the depths, until the posterior wall of the rectum is brought into view. The coccyx is
resected to permit a wider exposure. Displacing the cut-ends of the sphincter ani muscle
lateralwards, the lower rectum is freed from the vagina or prostate anteriorly and deliv-

ered posteriorly into the wound. Laterally, the levator ani muscles attached to the rectum are divided. By careful dissection posteriorly, laterally and anteriorly, the rectum is gradually delivered through the perineal wound and the reflection of the peritoneum brought into view. The peritoneum is incised concentric with its attachment to the bowel and the peritoneal cavity opened. With this step, and, particularly, if the patient has a long sigmoid loop, the sigmoid can be delivered through the perineum. A point on the sigmoid above the level of the lesion is selected which is to form the new anus and, at this point, the tissues making up the mesentery are divided and the bowel cleanly isolated. The peritoneum is reattached to the bowel at a higher level, closing the peritoneal cavity. The levator ani muscles, if they have not been too near the pelvic wall, are reattached to the
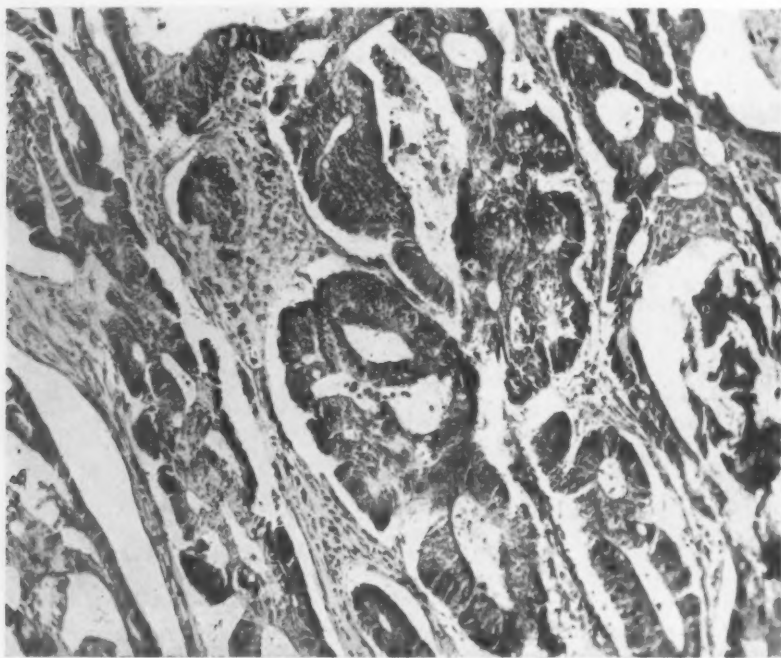


Fig. 4.—A field from the cecal carcinoma, which exhibits a multiacinar type of architecture, indicating considerable malignancy. For comparison with the illustration of the appendiceal carcinoma. (x 140)

intestine. The segment of delivered intestine is then swung forward within the sphincter ani muscle, the divided ends of which are then sutured with silk. The posterior wound is closed in layers with a rubber tissue drain placed in the pelvis along the curve of the sacrum. The intestine is cut across at the level of the skin and its cut-margins sutured to the skin as in the Whitehead operation. It is to be emphasized that the bowel, as reconstructed, should not be under the slightest tension so as to avoid the tendency to retraction upward into the pelvis.

A minimal infection of the dorsal aspect of the wound developed after operation, but promptly cleared under dakinization. The anal sphincteric control remained satisfactory.

*Specimen From Second Operation.*—This consisted of a segment of rectum and sigmoid, measuring 18 cm. in length and 12.4 cm. in circumference (Fig. 5). It is difficult to describe its appearance, as it was so thoroughly covered with polypi, of all sizes and shapes, that this would be unprofitable; the photograph is more informative. The polypi

grew in three main clumps, or crops, each of them some 9 cm. in axial and 7 cm. in circumferential diameter. They projected 5 cm. into the lumen. One bunch of tumors had a pedicle 5 cm. in length, 2 cm. in diameter and a cauliflower-like top, measuring 7x5x6 cm.

Sections from representative polypi in this specimen showed them to be well-differentiated adenomas without any evidence of carcinomatous change. Thus, they were dissimilar from the growths in and about the cecum.
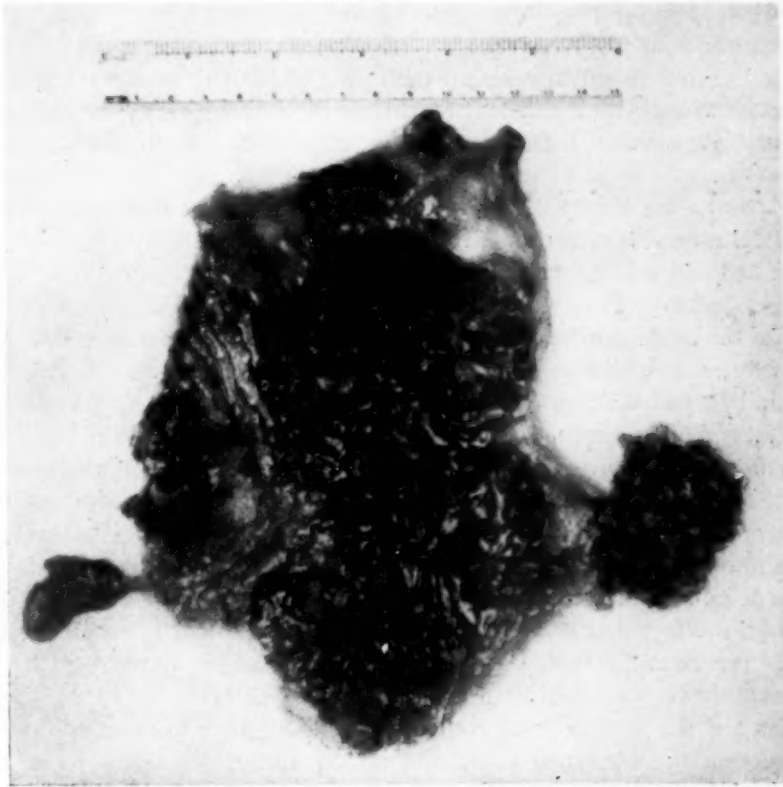


FIG. 5.—The rectum opened to show the polyposis of that organ. The two masses at the lower margins of the specimen represent the bisected portions of one large malignant adenoma. This was supported by a relatively tenuous pedicle.

*Subsequent Course.*—The patient left the hospital on the 118th day after admission, the transverse colostomy stoma having been closed on the 109th day. She has been followed in the Out-patient Department for two months; has gained 15 pounds in weight; feels much stronger; and, more importantly, has one normal bowel movement daily. Her anal sphincter is strong and effective, and there is no prolapse of the rectal mucosa. She exercises her sphincter once daily by performing digital massage for five minutes; this has been her practice during the two months since her operation.

DISCUSSION.—When the patient entered the hospital it was evident that she was a poor surgical risk and was in no condition for an immediate operation. Attempts to replace lost tissue-fluids and serum proteins, employing

amigen, whole blood and plasma, were futile because of the large amount of blood and proteins lost with each movement of the bowels. A transverse colostomy, as a first procedure, placed the rectum at rest and improved the patient while it also permitted the removal of polypi from the splenic and hepatic flexures for microscopic study. Inasmuch, as there was a reasonable suspicion of cancer in the ascending colon and since repeated biopsies of the rectal lesions were reported as nonmalignant, the former was attacked first. Careful preoperative preparation had cleared the ascites that existed at the time of admission.

The resected specimen revealed multiple polypi, both malignant and non-malignant, as well as a full-blown carcinoma of the cecum; in addition, a malignant adenoma of the appendix was found. This is unheard of in our experience.

Despite the proximity of the anastomosis of ileum and transverse colon to the left colostomy, movements of the bowels were controlled by means of a low residue diet and the administration of salts of bismuth.

A perineal-type of resection of the rectum and lower sigmoid, with preservation of the anal sphincter, was selected as the operation of choice in connection with her rectal lesions, as it was evident that the sigmoid was redundant and could be pulled down easily and the polypus-bearing area involved only the distal end of that segment of the colon. As biopsies from the polypi in this region invariably showed nonmalignant lesions, this type of operation was thought to be best calculated to overcome the patient's rectal symptoms and restore normal function. Whether the rectal prolapse was attributable to trauma to the sphincter during her several pregnancies or whether the polypoid mucosa acted as an intussusceptum and, thus, produced extrusion is not clear. Certainly, the fact that she had had a large rectocele and cystocele repaired and her cervix amputated, because of cervical prolapse, would suggest that weakness of the anal sphincter developed first, to be followed by chronic irritation and the production of multiple polypi. As there were polypi in equal abundance in the ascending colon and cecum, this explanation would seem faulty, and the hypothesis that prolapse was due to rectal polyposis appears to be more tenable.

Insofar as the carcinoma which occurred in this patient's appendix is concerned, the following points may be brought out; carcinoma of the appendix is a very rare condition, indeed, and a great deal of confusion has been caused by the inclusion of the so-called "carcinoids" in this category. Thus, when one endeavors to read up on the subject, many false clues are traced back, only to find that they lead to carcinoid tumors. Recently, Uihlein and McDonald,[1] of the Mayo Clinic, reported five cases of true adenocarcinoma of the appendix, the photomicrographic illustrations of which might have been taken from sections of the tumor reported in this paper. These authors divide appendiceal carcinoma into three categories, basing their observations upon an investigation of all the appendiceal carcinomas removed at the Mayo Clinic, between the years 1910 and 1941: There were 144 specimens of which 127 (88.2 per cent)

were carcinoids, 12 (8.3 per cent) were cystic carcinomas, and five (3.5 per cent) were colonic in type, resembling the adenocarcinomas of the colon. To the last category they added four new cases, bringing the number up to a total of nine, at the time of publication of their paper in 1943. These figures give an excellent idea of the rarity of the colonic type of appendiceal carcinoma. The authors have tabulated the usual sites of the various types; the colonic is found to arise in the base or tip of the organ and, occasionally, to invade the cecum. One of their recent cases, however, showed the tumor in the middle third of the organ.

Association with multiple polyposis, or carcinoma primary in the cecum, is not mentioned by these or other authors consulted; apparently, it is extremely rare. Ewing[2] dismisses the subject by remarking that appendiceal carcinomas are usually bulky adenocarcinomas that resemble those of the colon. Apparently, from reports which one may find on the subject, these tumors are usually well-differentiated; show a variable number of mitotic figures; and, may, on occasions, metastasize to lymph nodes and the liver. The Mayo group give them a Broder's grading of I, which would correspond with the histologic criteria in our case very excellently. Their group of "cystic carcinomas," in which there are malignant changes in the mucosa of an appendiceal mucocele, does not interest us here. One might question including it under true carcinomas, just as one might doubt the advisability of including argentaffin carcinoids in that category.

### SUMMARY

An unusual case of multiple polyposis of the colon, cecum, vermiform appendix and rectum is presented. There was marked prolapse of the rectum and the patient had become very much debilitated by loss of blood. This was successfully overcome by (a) preoperative supportive treatment; (b) careful timing of the operative procedures, including transverse colostomy, ileotransverse colonic anastomosis, hemicolectomy, perineal resection of the rectum, and lower sigmoid; and (c) closure of the stoma of the transverse colostomy.

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2 Ewing, J.: Neoplastic Diseases. Ed. 4, W. B. Saunders Co., Phila. and London, 1940. p. 725-726.

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# THE EFFECTS ON VENOUS ENDOTHELIUM OF ALTERATIONS IN BLOOD FLOW THROUGH THE VESSELS IN VEIN WALLS, AND THE POSSIBLE RELATION TO THROMBOSIS

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MOST CLINICIANS are increasingly conscious of the menace of venous thrombosis and possible pulmonary embolism. Why thrombosis occurs must surely be known before effective prevention of the possible results can be attained. It is to the end of determining causes of clotting in veins that these experiments have been undertaken. They are not wholly satisfactory, since in dogs there is no transition period between buoyant good health and progress to death as occurs in humans.

In this paper, the attempt has been made to introduce the circulation of the vein walls as a factor in the problem of thrombosis. This is a new approach and may be profitable.

When such lesions as so-called "spontaneous" thrombophlebitis or phlebo-thrombosis are discussed, it is assumed that three factors are relevant to their etiology, and that a given instance of "spontaneous" venous thrombosis or phlebitis is due to an imbalance of any two of them. These factors are (a) alterations in the quality or quantity of blood constituents; (b) alterations in the rate of flow of blood in the veins; and (c) alterations in the endothelial coats of the veins. This paper is devoted principally to a consideration of the last-named factor, the vein walls, and some of their physiologic relationships.

Experimentally, venous thrombosis has been produced by damaging vein walls in various ways, such as crushing, stretching, scratching off endothelium, or injecting sclerosing agents. These factors scarcely resemble any pathologic process which may occur in postoperative or postpartum patients, or in individuals afflicted with systemic infections, cardiovascular disease, or other debilitating disorders. A great amount has been written concerning the nutrition of the walls of arteries;[1] relatively little work has been done on the nutrition of vein walls. Discussions in the literature reveal three schools of thought: (a) that the inner layers of the vein wall are nourished by blood in the vasa venarum; (b) that the inner layers of the vein wall are nourished by blood in the parent lumen; and (c) combinations of these two.

No matter what the source or sources of vein-wall nutrition, it is probably necessary to distinguish between the supply of oxygen and the supply of other metabolic necessities, such as water, glucose, amino-acids, and inorganic salts. Such a distinction is advisable, for oxygen, unlike foodstuffs, must be constantly supplied since facilities for its storage in tissue or tissue fluid are

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practically nonexistent. Certainly, the organism as a whole reacts much more promptly to oxygen lack than it does to lack of nutriments, and if venous endothelium is at all comparable to capillary endothelium it should suffer from hypoxia in a somewhat similar fashion.

### THE ANATOMY OF VASA VENARUM

#### 1—TECHNIC

Since few investigators have studied the vascular supply to vein walls, it was necessary to spend much time on this topic. In the present work, the first attempts to demonstrate these tiny vessels involved the usual injection technics, which were only partly successful. A new technic was then devised for holding vein segments after they had been removed, and the benzidine staining reaction was employed to outline the vasa venarum. All experiments were carried out on dog veins. Depending on the size of the animal and the available length of the vein to be studied, a segment, 3 to 12 cm., was carefully
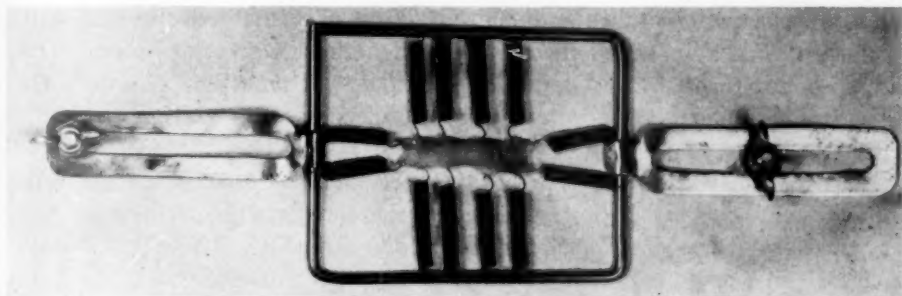


FIG. 1.—Apparatus used for holding vein segment flat while being stained, dehydrated, and cleared. The tissue is secured by the stainless steel springs in the frame made of stainless steel rod, which, in turn, is held by adjustable brass clips while the specimen is being attached.

dissected free, and a glass cannula inserted in its distal end and the lumen washed through with Ringer's solution at body temperature. Ligatures, which had been previously placed at either end of the isolated segment, were immediately tied, imprisoning Ringer's solution in the vein lumen. The segment was then removed, and kept moist with warm Ringer's solution while it was being opened longitudinally and stretched out flat in a rectangular frame by small springs (Fig. 1).

The frames used were made of stainless steel rod, 3.17 mm. in diameter, bent into rectangles 7 cm. wide and from 7 to 15 cm. long, the various lengths being necessary to accommodate various lengths of vein segments. The springs used were made of stainless steel wire 0.010 in. thick. Each spring consisted of 50 turns of wire, and was 2.2 cm. long and 4 mm. outside diameter. A linear force of 15.3 Gm. stretched a spring 1 cm. Simple loops lying in the same plane were bent on each end of a spring, and one or both loops were

sharpened to a fine point with a small motor-driven hand grinder so that they would easily pierce vein walls.

To eliminate excessive pull on the vein segment being mounted, the spring should not have too much tensile strength, and the frame size should not be unduly large in relation to the size of the specimen. To hold the frames steady while the vein segments were being attached to them, two adjustable clips of half-hard brass were mounted on a flat tray so that the curved tips of the clips could be fitted over the ends of the frames and locked in place by wing-nuts.

To mount a given vein, a rectangular frame of suitable size was placed on the flat tray, and the brass clips adjusted and locked in position to hold it in place. The portion of vein to be attached to the frame, having ligatures at each end and Ringer's solution in its lumen, was then placed on the tray within the frame, and kept well-moistened with warm Ringer's solution. The sharp end of a small spring was then thrust through the loose **cuff** of vein wall at each end, outside the ligatures. By means of small scissors and forceps, the vein segment was then opened longitudinally, care being taken that the point of the scissors within the lumen did not damage the opposite vein wall.

Once the vein is opened throughout its length, other springs were alternately hooked through the lateral edges of the wall on either side, and the outer, free end of each spring was attached to the side rod of the frame. These springs were placed 5 to 8 mm. apart.

Then each of the four corners of the specimen was attached to the ends of the frame by springs, after which the tissue contained in the ligature was cut off, removed from the spring holding it, and discarded. These two springs at either end were then hooked through the midpoint of the end of the vein segment. Once the tissue is thus secured, the entire frame was turned over, so that the endothelial surface of the vein faced downward. By means of scissors, forceps, and magnifying spectacles or a dissecting microscope, any clumps of excess adventitial tissue were dissected away. This was done so that the vein segment would be flat on a glass slide when finally mounted in balsam. It must be done with meticulous care lest the vasa venarum be damaged.

The entire preparation was then immersed in warm Ringer's solution and washed by gentle agitation for one or two minutes, after which a similar washing was carried out using 5 per cent dextrose. It is inadvisable to wash these specimens by directing running streams of solutions on them, for the force of the stream may damage the tissue. This is of utmost importance when the endothelium is to be stained and studied.

Each preparation was then immersed in a solution of benzidine for 15 minutes. A mixture suggested by Sjöstrand[2] was used. This was prepared by combining two solutions, as follows: Solution A contained 0.9 Gm. of benzidine base in 60 cc. of 95 per cent ethyl alcohol. Solution B contained 3 cc. of 30 per cent hydrogen peroxide in 120 cc. of 70 cent cent ethyl alcohol. Solutions A and B are then mixed, and the vein segments placed in this mixture.

FIG. 2.—Photomicrograph of blood vessels in wall of normal jugular vein of dog, stained with benzidine. (× 210)



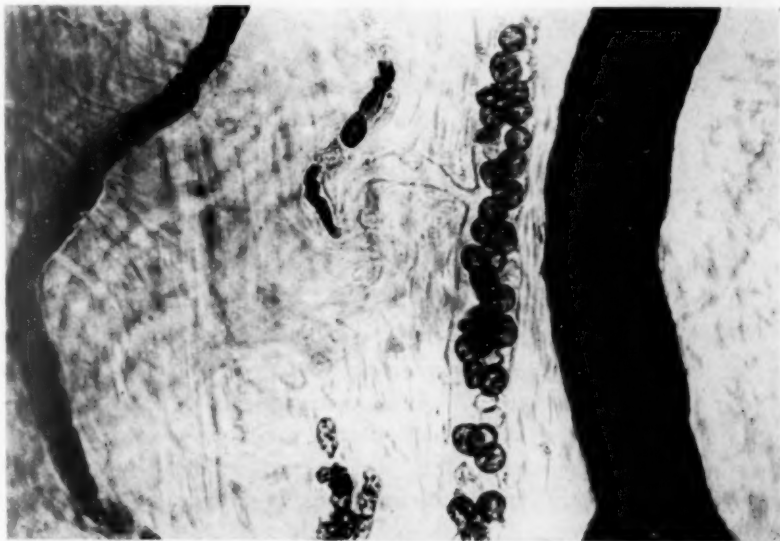FIG. 3.—A portion of Figure 2. (× 550). Note stained red cells in vessels and tortuous course of partly filled capillary.

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The benzidine, by selectively staining red blood cells, can outline the vessels in which they are contained. This technic, first used by Lepehne,[8] was later employed with various modifications by Sjöstrand,[2] by Pickworth,[4] by Campbell, Alexander, and Putnam,[5] and by others, to outline small blood vessels in sections of brain, spinal cord, and other viscera. It stains the blood cells an amber to dark brown color, depending on the duration of staining and the amount of blood present in a given vessel.

Each specimen was again washed in 5 per cent dextrose, and then fixed in 10 per cent neutral formalin for 12 to 18 hours, following which it was dehydrated by successive immersions in 70 per cent, 80 per cent, 95 per cent,
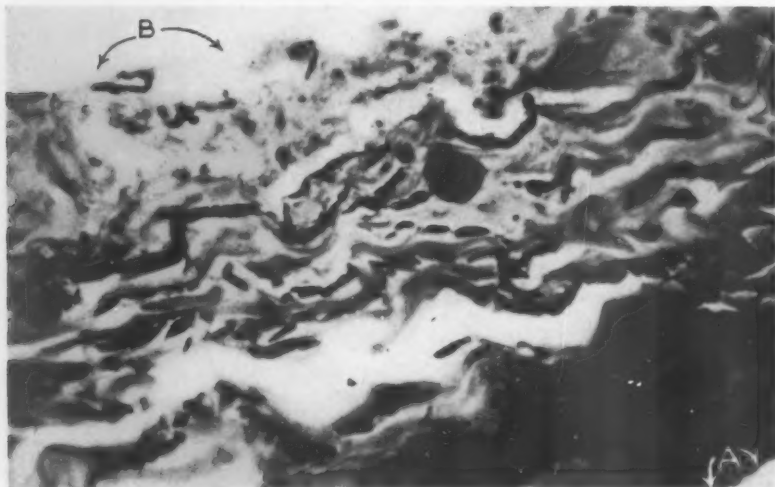


FIG. 4.—Cross-section of wall of normal jugular vein of dog, stained with benzidine and counterstained with hematoxylin and eosin. The endothelial surface is shown in the lower right corner (A), and the adventitial surface in the upper left corner (B). Cut-ends of three vasa vasorum are shown in the inner part of the adventitial coat.

and absolute alcohol, allowing it to remain one-half hour in each of the first three solutions, and one hour in the absolute alcohol. Clearing was carried out by immersion in oil of wintergreen for 12 to 18 hours.

As containers for the various solutions in which these preparations were immersed, rectangular glass dishes, ordinarily used for food storage in household refrigerators, served admirably. Their inside dimensions at the bottom are 19 cm. in length, 8 cm. in width, and 6 cm. in depth, and each is equipped with a glass cover.

After clearing, each specimen was removed from its frame, by securing the frame on the flat tray with the brass clips and cutting off the margins of the segment where the springs pierced it. The remaining portion of flat, stiff, transparent vein wall was then mounted in balsam between a glass slide and a long cover slip.

## 2—ANATOMY

Preparations so made admit of examination with a hand lens or a microscope, and a large area of vasa venarum can be studied by looking directly down upon it (Figs. 2 and 3). The vessels vary in diameter from those of true capillary size with diameters of 10 to 20$\mu$, to those of arteriole or venule proportions having diameters of 60 to 75$\mu$. An occasional arteriovenous anastomosis is visible. The richness of these plexuses is impressive, an opinion also expressed by Köster,[6] in 1875, who, in commenting on the structure of blood vessel walls and inflammation of veins, remarked: "The vasa nutritia (of veins) are extraordinarily more numerous than is ordinarily represented, and supply quite small veins, whose wall one thinks would surely be without vessels."
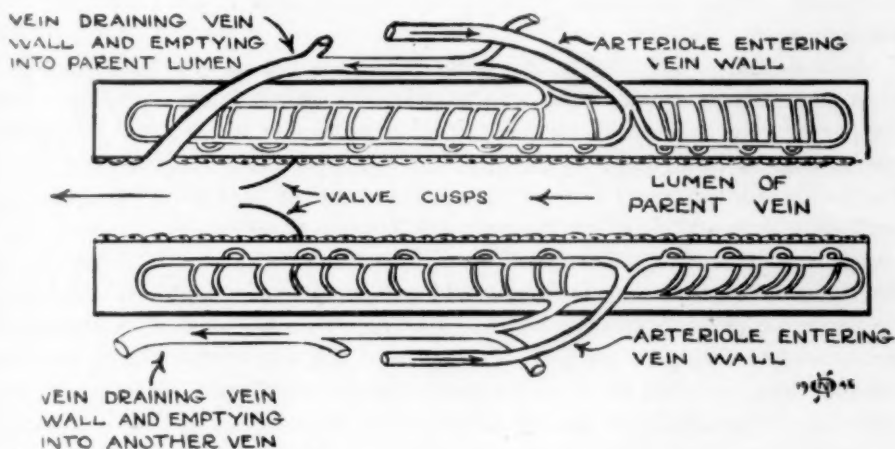


Fig. 5.—Diagram of blood vessel pattern in vein walls.

In specimens so studied, vasa venarum have not yet been seen in the media or in the intimal layers of the vein wall (Fig. 4). This justifies no conclusions, however, that tiny vessels do not penetrate into the media or intima, for demonstration of such vessels may be prevented by lack of penetration of the benzidine stain deeper than the inner part of the adventitia, or because certain vessels are empty at the time of staining. It may well be that staining for longer periods will permit greater dye penetration and, consequently, outline vessels in the deeper vein layers.

Study of the patterns of blood vessels in vein walls have led to certain concepts about their origin, distribution, and destination. As diagrammed in Figure 5, they arise as branches from arterioles present in perivenous connective tissue, these arterioles, in their turn, having come from neighboring arteries. The arteriolar vasa venarum enter the venous adventitial coat, and then divide and subdivide to form a rich capillary network whose depth of penetration is still uncertain. It is important that in all specimens so far

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studied there is no evidence that the venous capillaries or the venules in the plexuses in vein walls empty directly into the parent lumen, but, rather, that the venous capillaries form venules which emerge from the adventitia of the vein wall usually as venae comites for the entering arterioles, and then empty into the veins which run in the loose perivenous connective tissue. These veins, in turn, then join others in the vicinity, and finally empty as a true tributary into some other vein, or, if it be in an extremity, it may empty into the parent vein at some more proximal site.

A consideration of the pressures acting within and around a vein attest to the efficiency of such a plan. If venous capillaries in the vasa venarum of a vein wall drained directly into the parent lumen, their emptying would be hindered by any local increase in intravenous pressure, and, unless they were all valved, actual regurgitation might occur into them if local intravenous pressure rose.

In a system so arranged that venous vasa venarum in vein walls emerge from the adventitia, and drain into surrounding veins, later emptying into the parent vein at some distant site, local increases in intravenous pressure can have no harmful, and may actually have a helpful effect on their emptying. For a rise in intravenous pressure in a given vein segment may, by exerting force on a vein wall from within outward, tend to massage blood out of the venous vasa venarum, and since they can drain into surrounding veins in a plexiform arrangement, their flow would not be seriously hampered. Again, if contraction of local muscle compressed a given vein segment, such pressure would tend to empty the veins in the vein wall and perivenous tissue, and at the same time force the blood in the parent lumen centralward. Thus, venous vasa venarum would have no obstruction put in their way, and their drainage might even be aided by an aspiration effect occurring at the site where the tributary they help to form opens into the parent vessel.

### CHANGES IN ENDOTHELIUM FOLLOWING ALTERATIONS IN BLOOD FLOW IN VASA VENARUM

An anatomic discussion of vasa venarum should be complemented by further studies to learn something of their function, particularly the part they play in vein wall nutrition. Accordingly, experiments were devised to study the effect on vein walls, principally on the endothelium, when the blood supply *via* the vasa venarum was cut off. It is not a difficult matter to dissect a vein segment free from all its surrounding tissues, to permit the vein to lie thus isolated for varying periods of time, and then to study the endothelial changes which may have occurred. In such experiments the dissecting technic must be meticulous in order that the effects of trauma will be kept to a minimum. Second, when a vein is carefully isolated, the nerves and lymphatics as well as blood vessels of the vein wall are divided. Third, if such studies of endothelium relied upon orthodox cross-sections only, it would be difficult to visualize in proper perspective a sufficient expanse of endothelium to derive an adequate picture of any changes which might occur. For this reason a new

approach was employed, and the vein walls mounted flat so that the inner layers could be examined microscopically after staining with silver nitrate.

When the time arrived for the termination of each experiment, a right-angled cannula, as wide-mouthed as the vein would admit, was inserted into the proximal end of the isolated vein segment, and the blood emerging from the vein was collected so that it could be immediately examined for clots, and minute volume determined and compared to normal flow. These vein segments were not washed out with Ringer's solution, lest endothelium be artificially damaged. They were ligated at either end, removed, opened longitudinally, and mounted flat in the small frames as previously described. Excess adventitia was trimmed away, and the segments were washed in Ringer's solution and 5 per cent dextrose, as discussed above. The Ringer's solution was used to remove any blood from the endothelial surface, and the 5 per cent dextrose, which was preferred to distilled water because it is isotonic, was used to wash away any chlorides remaining from the Ringer's solution and, thus, prevent the formation of silver chloride when the silver nitrate was applied.

Since, in these segments, the endothelium and not the vessels in their walls was to be examined, they were stained with 1 :250 silver nitrate solution. To do this, each frame was placed over a beaker or Petri dish, and a few drops of silver nitrate placed gently on the endothelial surface so that it would not run on to the lower or adventitial surface. The stain was permitted to remain 30 to 60 seconds, the vein segment being gently agitated during this time. It was not found necessary to formally expose the vein to a source of ultraviolet light after applying the silver nitrate. Sufficient staining of intercellular lines occurred even when the silver nitrate was applied at night under artificial light.

The staining was followed in each instance by fixation, dehydration, clearing, and mounting in balsam, as previously described.

With this technic a large flat area of endothelial surface can be examined microscopically by looking directly down on it, and it has often been possible to examine 5 sq. cm. of endothelial surface in one preparation—more than could be studied in several thousand cross-sections made by the usual microscopic technic.

So far as is known, this approach to the study of venous endothelium has not been previously employed. Langhans,[7] in 1866, did make mention of horizontal sections used in studying aortic endothelium, but details of how he made his preparations are lacking. He also stained these specimens by immersing them from 5 to 24 hours in 0.4 per cent solution of silver nitrate. This salt was first employed as a tissue stain by Flinzer,[8] who, in 1854, used it to outline the cells of the cornea, but, according to Mann,[9] silver staining was made a general histologic method by von Recklinghausen in 1860. Since that time it has been used in various ways by various investigators. The general principles, as well as the technical details of its use, have been summarized by Ranvier,[10] by Mann,[9] and by Lee.[11]

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When applied to venous endothelium, silver nitrate stains the intercellular cement substance a dark brown to black color, which Rabl[12] has suggested is due to the formation of a silver proteinate. He feels that it was not metallic silver, for it was soluble in sodium hyposulphite. In normal endothelium, the cells themselves do not usually stain, but they are nicely outlined and form a delicate mosaic pattern (Figs. 6 and 7).

Normal venous endothelium apparently varies somewhat in its appearance. The intercellular lines may vary in thickness; nuclei of the endothelial cells are sometimes visible, and whether this is due to their being stained, *i.e.,* a positive shadow, or due to their not being stained while cytoplasm is stained, *i.e.,* a negative shadow, is not clear. In some preparations where the vein wall has not been damaged, fine, roughly parallel lines running transversely to the long axis of the vein are visible through a superimposed endothelial pattern. At the present time, these are believed due to the silver nitrate solution penetrating through the endothelial layer and staining some cement-like substance or ground substance between the circular muscle fibers. Some of these variations may be associated with variations in the nutrition or age of the dogs used, differences in oxygen saturation of venous blood, and inequalities in technic in removing and staining the venous segments.

The first series of experiments to be discussed is concerned with changes in the inner layers of the wall in veins which are not obstructed but which are dissected free from all blood supply to their walls. After gently separating a vein from all its surrounding tissues, the line of cleavage being in the inner part of the adventitia, rubber dam is sutured loosely around the isolated portion to make certain that it remains separated from its bed. The wound can then be closed and the vein permitted to remain *in situ* for periods varying from three to 48 hours.

When such an experiment is continued for six hours, and the vein segment removed, stained, and mounted as described, the inner coats, when viewed microscopically at low power (Fig. 8), show some areas where the endothelium looks little, if at all, different from normal. However, it is more granular, many neuclei are visible, and they have the appearance of negative shadows. At various places, round black spots occur on the intercellular lines, their greatest incidence being at junction points. In other areas, the endothelial pattern is absent, being replaced by roughly parallel black lines which run at right angles to the long axis of the vein. In some instances endothelial loss is focal, consisting of absence of only a few cells, the space being filled with the black parallel lines or with a homogeneous black area studded with small round vacuole-like structures. These clear tiny circular structures have not yet been identified. The black transverse lines, however, are felt to represent some substance lying between circular muscle fibers, possibly similar to intercellular cement or ground substance, and which has been stained black by the silver nitrate, because the overlying endothelium has desquamated, allowing the silver to come in direct contact with it.

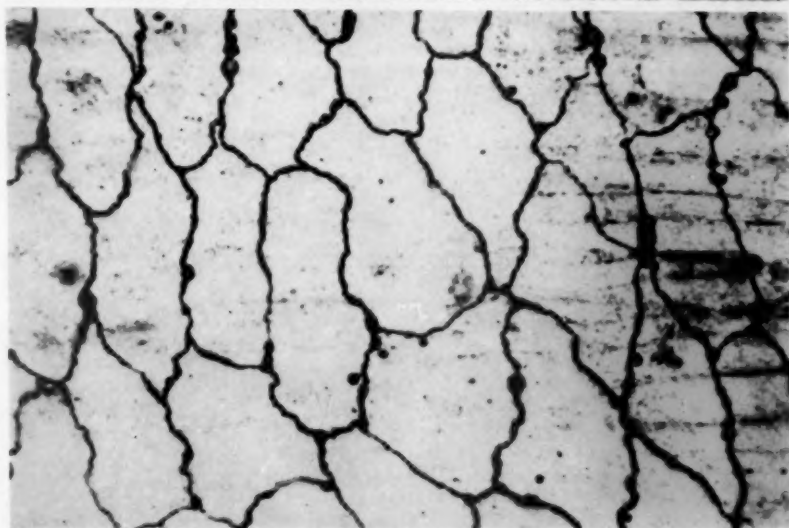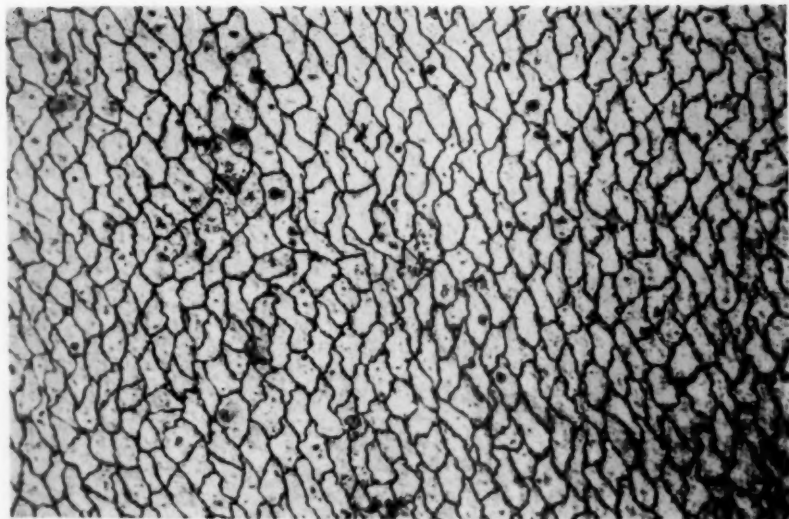Consideration has been given to the suggestion that where the black

Fig. 6



Fig. 7

Fig. 6.—Photomicrograph of the endothelium of a normal jugular vein of a dog, stained with 0.4 per cent silver nitrate solution. ($\times$ 210). Irregular black granular deposits are present in some areas. The round black shadows present on some cells are not nuclei but probably masses of protein material stained with silver nitrate. An occasional nucleus is visible as a round, relatively light zone.

Fig. 7.—A higher magnification ($\times$ 550) of a portion of Figure 6. Note the round, relatively light cell nucleus in the right upper part of the picture, as well as the variation in the width of intercellular lines. A few black parallel lines are seen beneath the endothelium, running at right angles to the long axis of the vein wall.
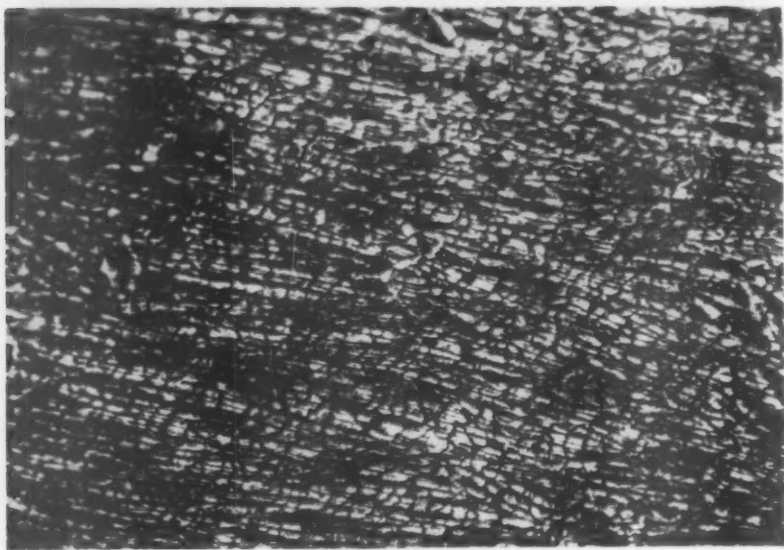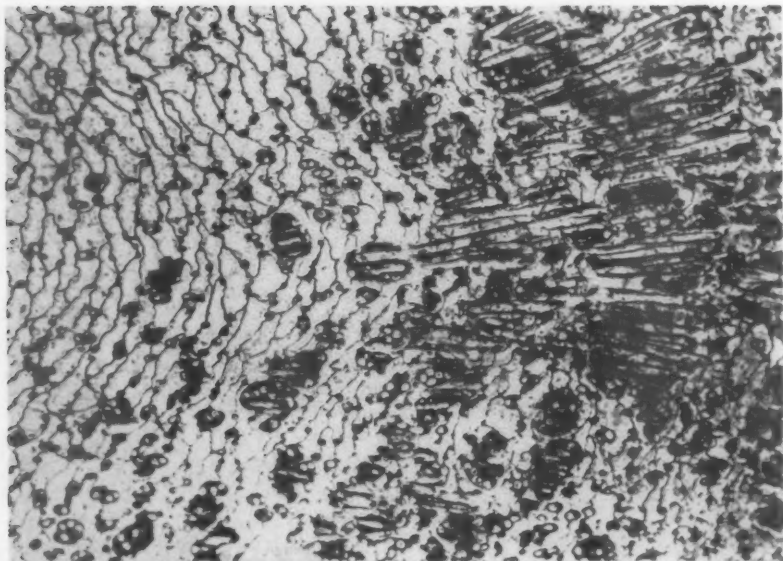
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F<small>IG</small>. 8



F<small>IG</small>. 9

F<small>IG</small>. 8.—Photomicrograph of endothelium of dog's jugular vein after the vein segment had been isolated from all blood supply to its wall for six hours. Stained with 0.4 per cent silver nitrate solution. ($\times$ 210)

F<small>IG</small>. 9.—Photomicrograph of endothelium of dog's jugular vein after the vein segment had been isolated from all blood supply to its walls for 13.5 hours. Stained with 0.4 per cent silver nitrate solution. ($\times$ 210). Black parallel lines, running at right angles to the long axis of the vein, are visible beneath the endothelial outline.

parallel lines are visible and endothelial cells are not, the phenomenon may be due simply to dissolution of cement substance, allowing the silver stain to penetrate through and react with the subendothelial tissues, leaving behind the unstained and, therefore, invisible endothelial cells, and that the observer may, thus, get the erroneous impression that the cells were absent. That these cells have desquamated is conclusively shown in conventional cross-sections of the vein walls.

In another experiment, continued for 13.5 hours, the endothelium was apparently still present, but the black transverse lines could be seen lying beneath it (Fig. 9). It seems possible that, in this particular vein, the silver nitrate penetrated through and between the endothelial cells, and stained some substance between the circular muscle fibers. In some areas, the cell nuclei are visible while in other areas they are not, yet in all places the subendothelial tissues are uniformly stained. It is reasonable to conclude that in some sites the silver nitrate passed through the cell bodies on its way to deeper layers, staining nuclei or cytoplasm *en route,* while in other sites the stain passed between endothelial cells, and did not enter them, for intracellular structures are unstained.

Apparently, when venous endothelium is deprived of the blood supply in the vein wall, it may react in two ways. It may desquamate, or some change in permeability to silver nitrate may take place which permits the stain to penetrate it. The suggestion immediately arises that desquamation may be a sequel to some alteration in permeability, allowing fluid to pass through the endothelium and accumulate beneath it, and, thus, lift it off. If this were true, then all endothelium remaining in veins isolated for more than six hours would show subjacent black transverse lines. This does not occur, for in a similar experiment continued for 24 hours and where the endothelium has desquamated in many areas, the clumps of cells which do remain show no black transverse lines beneath them, indicating that desquamation was the principal change rather than some alteration in permeability to silver nitrate (Fig. 10).

Where this process is continued for almost the same time, *i.e.,* 23 hours, in another animal, only a few isolated endothelial cells remain, the surface otherwise showing only the black transverse lines (Fig. 11).

If such an experiment is continued for 40 hours, the inner surface of the vein, when examined microscopically, is devoid of endothelial cells, the entire segment being lined by circular muscle fibers (Fig. 12). When viewed in cross-section, the endothelium is absent, and the blood in the lumen is seen to be in most intimate contact with the muscular coat of the vein wall. This lumen did contain a small adherent clot.

These specimens, along with many others from similar experiments conducted for varying periods up to 48 hours, indicate that when vein segments are isolated but unobstructed, the first changes that occur (usually in four to six hours) are either focal desquamation or some change in permeability to silver nitrate, and that the desquamation increases as the period of isolation lengthens, becoming complete in some veins in 23 hours.
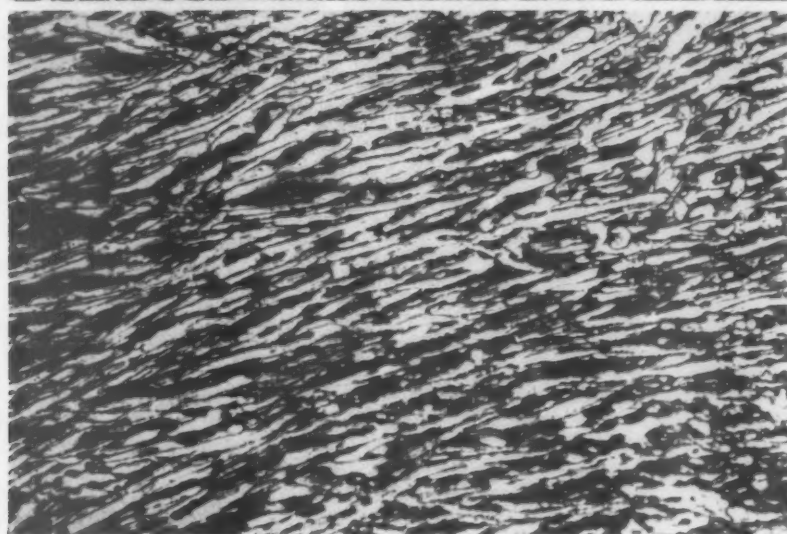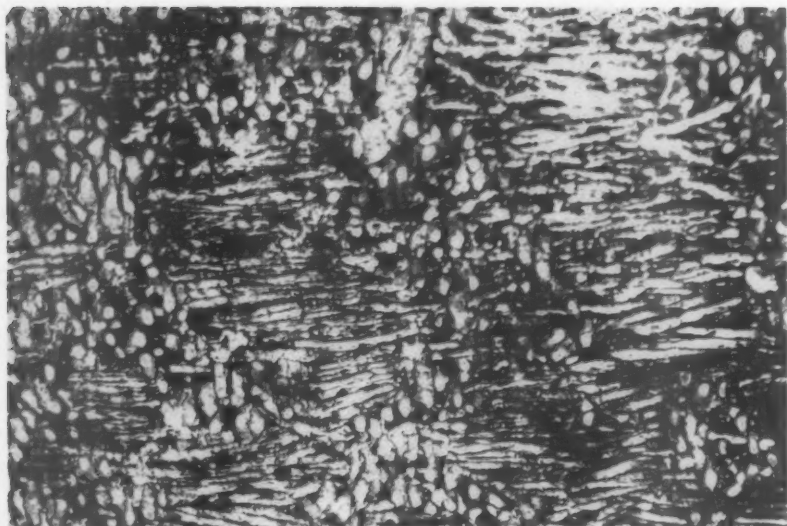
FIG. 10



FIG. 11

FIG. 10.—Photomicrograph of endothelium of dog's jugular vein segment after the vein had been isolated for 24 hours from all blood supply to its wall. In areas where the endothelial pattern is absent, the black transverse lines are seen. Many nuclei of endothelial cells appear as relatively light areas. Note that where the endothelial pattern is still present, no transverse lines are visible beneath it.

FIG. 11.—Photomicrograph of endothelium of dog's jugular vein segment after the vein had been isolated for 23 hours from all blood supply to its walls. Only a few isolated endothelial cells remain, the remaining surface being probably composed of smooth circular muscle. Stained with 0.4 per cent silver nitrate solution. ($\times$ 210)

FIG. 12
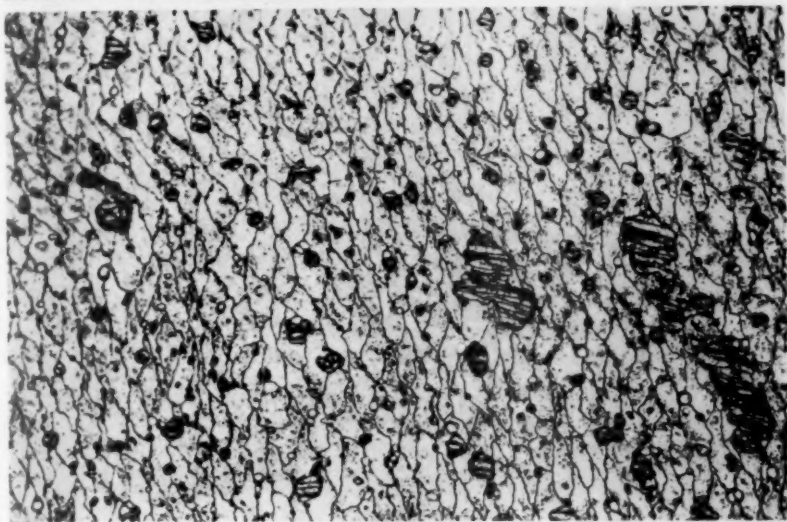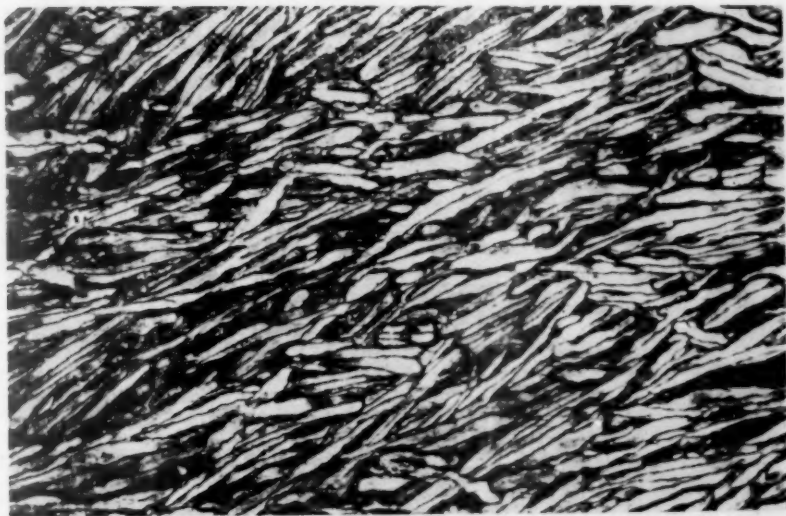


FIG. 13

FIG. 12.—Photomicrograph of endothelium of dog's jugular vein segment after vein had been isolated for 40 hours from all blood supply to its wall. All endothelium has desquamated, leaving a layer of smooth muscle. Stained with 0.4 per cent silver nitrate solution. ($\times$ 210)

FIG. 13.—Photomicrograph of endothelium of dog's jugular vein segment after nine hours of partial obstruction of blood flow through the lumen. Stained with 0.4 per cent silver nitrate solution. ($\times$ 210). The endothelium appears granular, and desquamation is focal.

It is noteworthy that as long as the blood flow in the parent lumen is unobstructed, intravascular clotting seldom occurs, even though endothelial desquamation is maximal. This is strikingly demonstrated by the gross appearance and behavior of these veins after they have lain isolated for over 12 hours. The vein segment under these conditions decreases by as much as 50 to 60 per cent in diameter, probably due to tonic contraction of circular muscle, and the minute volume of blood flow through it is about 25 to 35 per cent of the original. This was determined by placing a wide-mouth, right-angle cannula in the proximal end of each segment before it was removed for mounting, and carefully measuring the minute volume outflow and examining it for clots.

Although minute volume of flow was lessened, the associated decrease in diameter of the vein helped to maintain the velocity of blood flow at a rapid rate, and it is probably this maintenance of velocity that prevented thrombosis, even in the presence of what are commonly termed "raw" surfaces, which in these instances were surfaces lined by muscle, a tissue whose ability to produce thromboplastin has long been respected. These experiments serve to reëmphasize the importance of stasis as a factor in the etiology of venous thrombosis.

It can, thus, be definitely demonstrated that division of all blood vessels, lymphatics, and nerves to a given segment of vein wall can, over a period exceeding four to six hours, result in increasing degrees of endothelial desquamation.

### CHANGES IN VENOUS ENDOTHELIUM ASSOCIATED WITH PARTIAL STASIS IN THE PARENT LUMEN

When the experiment is varied so that partial stasis is produced in a vein without severing the vasa venarum, the resulting endothelial changes in the endothelium just distal to the obstruction are similar in type but less marked in severity. Slowing of blood flow was brought about by placing small metal clamps with clearances of 0.75 mm. around the proximal part of a femoral or external jugular vein and permitting them to remain thus for periods ranging from nine to 75 hours. Measurements of minute volume with and without such clamps in place indicate that they reduce blood flow in the parent lumen by 80 to 90 per cent of normal.

When such a clamp remains in place nine hours, and the vein segment distal to it is then removed, stained, and mounted as previously described, the endothelium shows minimal damage (Fig. 13), represented by a granular appearance of the endothelium, the presence of an increased number of nuclei and focal endothelial desquamation. A thrombus not attached to the vein wall was present in this vein at the time of removal.

If the slow blood flow is allowed to persist for 29 hours, the endothelium presents minimal to moderate damage (Fig. 14). In the flat preparation of vein wall from which the illustration was made, there are very large areas showing no damage, and a few areas wherein the endothelium has desquamated. There was a clot lying free in this vein lumen at the time of removal.

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Fig. 14



Fig. 15

Fig. 14.—Endothelium of dog's jugular vein after 29 hours of partial obstruction of blood flow in the lumen. Stained with 0.4 per cent silver nitrate. ($\times$ 210). The endothelium is quite granular, and several areas of desquamation are visible.
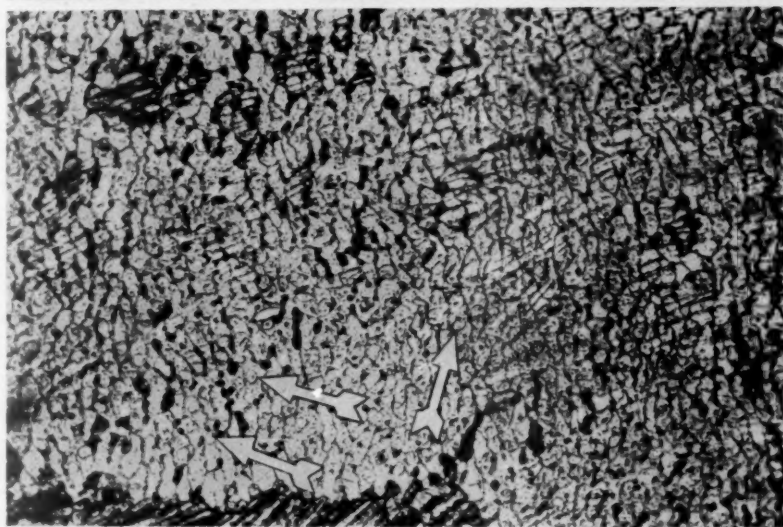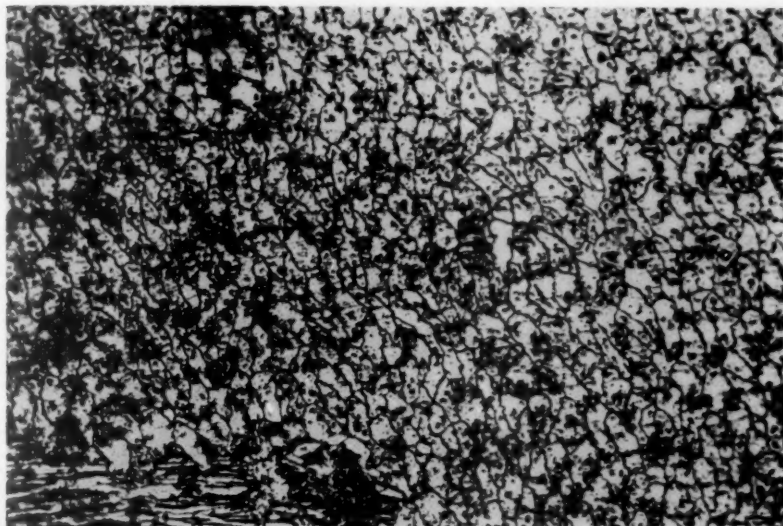
Fig. 15.—Endothelium of dog's jugular vein after 74 hours and 40 minutes of partial obstruction of blood flow in the lumen. Stained with 0.4 per cent silver nitrate. ($\times$ 210). Transverse lines are visible through the endothelium. Some endothelium has desquamated, and many nuclei are visible.

Experiments conducted in a similar way for 75 hours result in endothelial permeability to silver nitrate in other areas, for the cells are absent in some zones, the nuclei are prominent in other zones, while in still other places black transverse lines can be made out with endothelial cell outlines present above them (Fig. 15). There was no clot present in this instance, but the decrease of blood flow was not quite as great as in the two previous veins.

In comparing results in the two sets of experiments, namely, isolation of veins without any obstruction, and partial obstruction without isolation, it is justifiable to conclude that isolation without obstruction causes much more endothelial damage, while partial obstruction without isolation, although not as destructive of endothelium, is a slightly more frequent cause of intravenous clotting for the time-periods during which these experiments have been conducted.

The objection may occur that, although stasis may well be present, for example, in the lower leg veins of many bedridden patients, there is little reason to feel that circulation through the vasa venarum has been cut off. This is true. But a variety of disorders may result in decreased oxygen supply to such vein walls. To enumerate some of them: hypoxia from deep or prolonged anesthesia or narcosis; any interference with pulmonary ventilation; poor oxygen transportation as in some cardiovascular diseases; occlusive arterial disease of extremities; or diminished blood flow to a resting or immobilized limb.

Given low oxygen values in arterial blood entering an extremity, both the blood nourishing the walls of the veins as well as the blood returning in the vein lumina may have proportionate decreases in their respective oxygen levels. It is conceivable that, under such conditions, venous endothelium is caught in the middle, between two poor oxygen sources whose total supplies are scarcely adequate to keep it intact. Add, then, stasis, which means allowing time, and a clot may promptly form. Such a theory, which may or may not operate clinically, leads to the proposal that, if it were sound, one should be able to produce venous thrombi consistently in experimental animals either by isolation and partial obstruction of vein segments, or by causing hypoxia plus obstruction of certain vein segments.

There is some evidence, as yet not conclusive, that experimental thrombi will regularly result in vein segments from a combination of isolation and partial obstruction of those segments, provided that sufficient time is allowed during which these factors operate. In nine experiments so conducted for varying lengths of time, thrombosis occurred in four instances where isolation and partial obstruction were present for more than 24 hours, but in only one instance of five where these conditions existed for less than 24 hours. In the animals where thromboses occurred, the experiments were conducted for 24, 25, 30, and 50 hours, respectively. Thrombosis occurred once in an experiment of three hours' duration, and not at all in four experiments carried out for 2, 12, 14, and 19 hours, respectively.

Much more experience with this approach to the study of vein walls is

required. It is not known whether old animals are more susceptible than younger ones to interference with vasa venarum, and observations so far made regarding this have been very limited due to the difficulty of securing old dogs. Studies will be continued using material obtained clinically where the past history, age, and general condition of the patient can be determined more accurately. Various counterstains will be utilized to permit more accurate interpretation of endothelial changes and to study other physiologic functions of vein walls.

The original suggestion to approach the study of spontaneous venous thrombosis by studying the nutrition of vein walls in flat preparations was made by Dr. Cecil K. Drinker. For the opportunity to work on these problems in his laboratory and for his innumerable kindnesses and suggestions, as well as those afforded by his staff—the Misses de Jony, Hardenbergh, Ordway, and Puleo, and Mr. Louis Freni—I am deeply grateful.

## SUMMARY

A new technic is presented for the use of dilute silver nitrate solution in staining and studying the inner coats of vein walls.

A new technic is presented for mounting flat segments of vein walls so that the inner coats of the wall can be stained and studied.

Use of the benzidine stain for outlining the vascular plexus in vein walls is described, and the distribution of these vasa venarum is discussed.

Changes in the inner coats of vein walls following isolation, obstruction, and a combination of isolation and obstruction of vein segments are discussed.

Theoretic connections between anatomy and physiology of vasa venarum, alterations in endothelium, and clinical venous thrombotic lesions are discussed.

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# DUPLICATIONS OF THE ALIMENTARY TRACT*

## REPORT OF SIX CASES

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DUPLICATIONS are rare developmental anomalies which are found in relation to any portion of the alimentary tract, usually the small intestine. They may be spherical or tubular and vary considerably in size but closely resemble the gastro-intestinal structures, their walls being made up of mucous membrane, smooth muscle and serosa. Duplications are usually discovered in infancy and childhood and they are of clinical importance because of the serious symptoms which they may produce.

Many names have been given to this malformation. In order to simplify the nomenclature, we are in agreement with Ladd[19] and include the terms "enterogenous cyst," "enteric cyst," "inclusion cyst," "ileum duplex," "giant diverticulum" and "unusual Meckel's diverticulum" under the general classification of "duplications of the alimentary tract." Although found in different locations and in different shapes and sizes, they are embryologically associated and should be grouped together. They should not be confused with Meckel's diverticulum, which is an entirely different abnormality with a distinct embryologic derivation.

Six cases of duplication of the gastro-intestinal tract were encountered at Babies Hospital between April, 1945 and November, 1946. All of them came to operation.

## CASE REPORTS

**Case 1.**—J. R., a 12-year-old white boy, was admitted to Babies Hospital, April 13, 1945 because of severe bleeding per rectum and weakness. On the morning of admission, he awoke feeling well, went to the bathroom for a bowel movement and passed a considerable quantity of fresh blood with his stool. He called to his mother and fainted. Four hours later he was brought to the hospital. There had been no previous episode of gastro-intestinal bleeding. The personal and family histories were noncontributory.

Examination on admission revealed a pale, apprehensive child with cold, clammy extremities. The pulse was 84, respirations 30, temperature 98.6° F. and blood pressure 94/40. The other physical findings were normal except for the presence of fresh blood in the rectum. A transfusion of 500 cc. of whole blood was administered, and proctoscopic examination performed one hour after admission. No abnormality was found, but fresh blood was seen coming from above the tip of the proctoscope. After the transfusion, the hemoglobin was 10.2 Gm. and the red blood cells 3,720,000. The leukocyte count was 11,000, with 68 per cent polymorphonuclear cells, 30 per cent lymphocytes and 2 per cent eosinophils.

During the ensuing four days he improved; there was no gross bleeding but the stools remained tarry and gave 4-plus reactions to the guaiac test. He was asymptomatic and maintained his hemoglobin and red blood count at about the same levels. On the 5th

hospital day, roentgenologic examination of the colon by means of a barium enema was done and no abnormalities were demonstrated. The barium was returned containing gross blood. The hemoglobin dropped to 7.2 Gm. (48 per cent) about seven hours later and he received another transfusion of 500 cc. of whole blood. After the 11th hospital day the stools became normal, and roentgenographic study of the gastro-intestinal tract was carried out after barium meal. Nothing abnormal was demonstrated.

*Operation.*—Celiotomy was performed, May 9, 1945, under ether anesthesia. The pre-operative diagnosis was Meckel's diverticulum, with ulceration and hemorrhage. About 15 cm. proximal to the cecum a small duplication of the ileum was found. It projected from the mesenteric side of the bowel, measured 3 x 2 x 2 cm. and extended out between the leaves of the mesentery plate (Plate IA). A segment of bowel containing the duplication, and extending 2 cm. above and below it, was resected. The patient made an uneventful recovery, and was discharged on his 14th postoperative day.

Follow-up.—A few months after operation he received radiotherapy for keloid formation in the scar. When last seen, November 22, 1946, 18 months postoperatively, he was asymptomatic.

*Pathology.*—The specimen consisted of a segment of ileum measuring 7 cm. in length. From the midportion projected an ovoid, soft, pale yellow structure 3 x 2 cm. (Plate IA). It was attached by a broad base, 2 cm. in diameter, to the mesenteric side of the bowel. On section (Plate IB), the cavity of the duplication was shallow and the lateral walls resembled intestinal mucosa. The mucosa was pale and spongy.

Microscopically (Fig. 1), portions of the internal surface were covered by intestinal mucosa as evidenced by villi and intestinal glands containing Paneth cells. Contiguous to the intestinal mucosa there were areas where the surface was lined by tall columnar, eosinophilic epithelial cells, and deeper in the mucosa there were many gastric glands. In some regions parietal cells predominated. A few clusters of Brunner's glands were also present. In one part, there was a deep ulcer. Its base was covered by eosinophilic material and the wall, including muscularis, was entirely replaced by granulation tissue which extended into the submucosa and serosa of the bowel lateral to the ulcer.

**Case 2.**—P. K., a 3.5-months-old white male, was admitted to Babies Hospital, December 21, 1945 with a history of pallor and tarry stools of five weeks' duration. At the age of two months he first passed a small amount of fresh blood per rectum. Subsequently, the stools became tarry and remained so until admission. At the age of three months a gastro-intestinal roentgen series and a barium enema, done at another hospital, were reported as normal.

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PLATE I

A.—Case 1: Duplication of ileum protruding from mesenteric side.

B.—Case 1: Inner aspect of duplication showing hyperplastic gastric mucosa which forms a contrast to the normal intestinal mucosa of the ileum.

C.—Case 2: The orifice by which the duplication communicates with the ileum is indicated by scissors and lies at the lower (distal) end of the accessory bowel. The duplication runs proximally along the mesenteric side of the ileum, between the leaves of the mesentery, for a distance of 10 cm. and then lies free. The dilated middle portion is lined with gastric and small intestinal mucosa and an ulcer is visible. The rounded enlargements near the free extremity are lined with gastric mucosa, while the mucosa of the narrow portion between them was found to resemble common bile duct mucosa.

D.—Case 4: A duplication lined with gastric mucosa. The external fistula is shown in the upper left corner of the specimen.

E.—Case 5: The duplication lies within the mesentery in close approximation to the ileum.
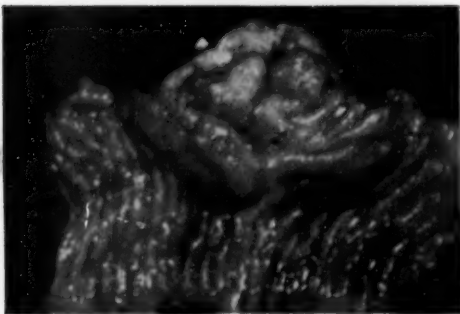
F.—Case 6: The duplication lies within the mesentery in apposition to the normal intestine and communicates with it at the lower end.

G.—Case 6: The mucosa of the duplication bears thick irregular folds resembling gastric mucosa. That of the small intestine bears transverse folds suggesting the valvulae conniventes of jejunum, as in Case 2, Plate IC.
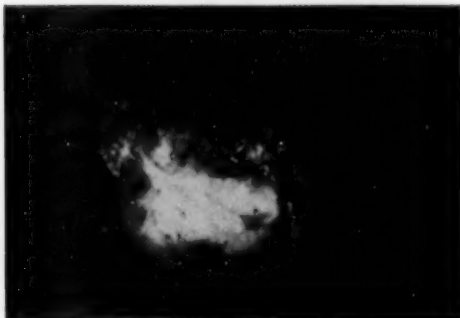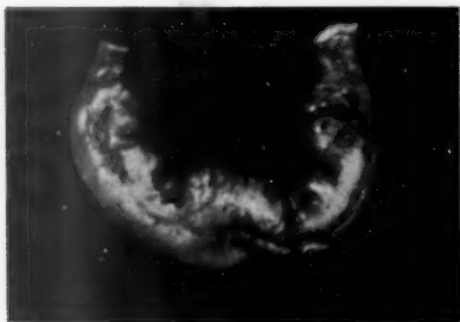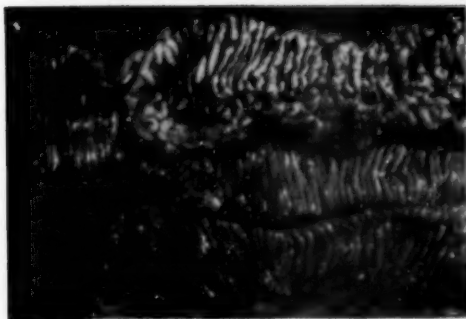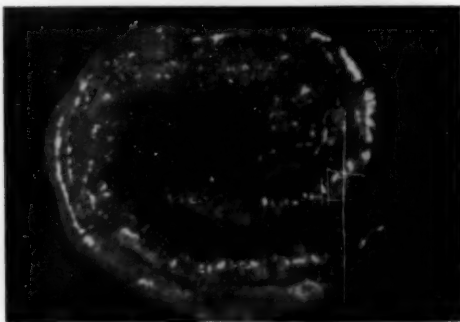
A

B

C

D

E

F

G
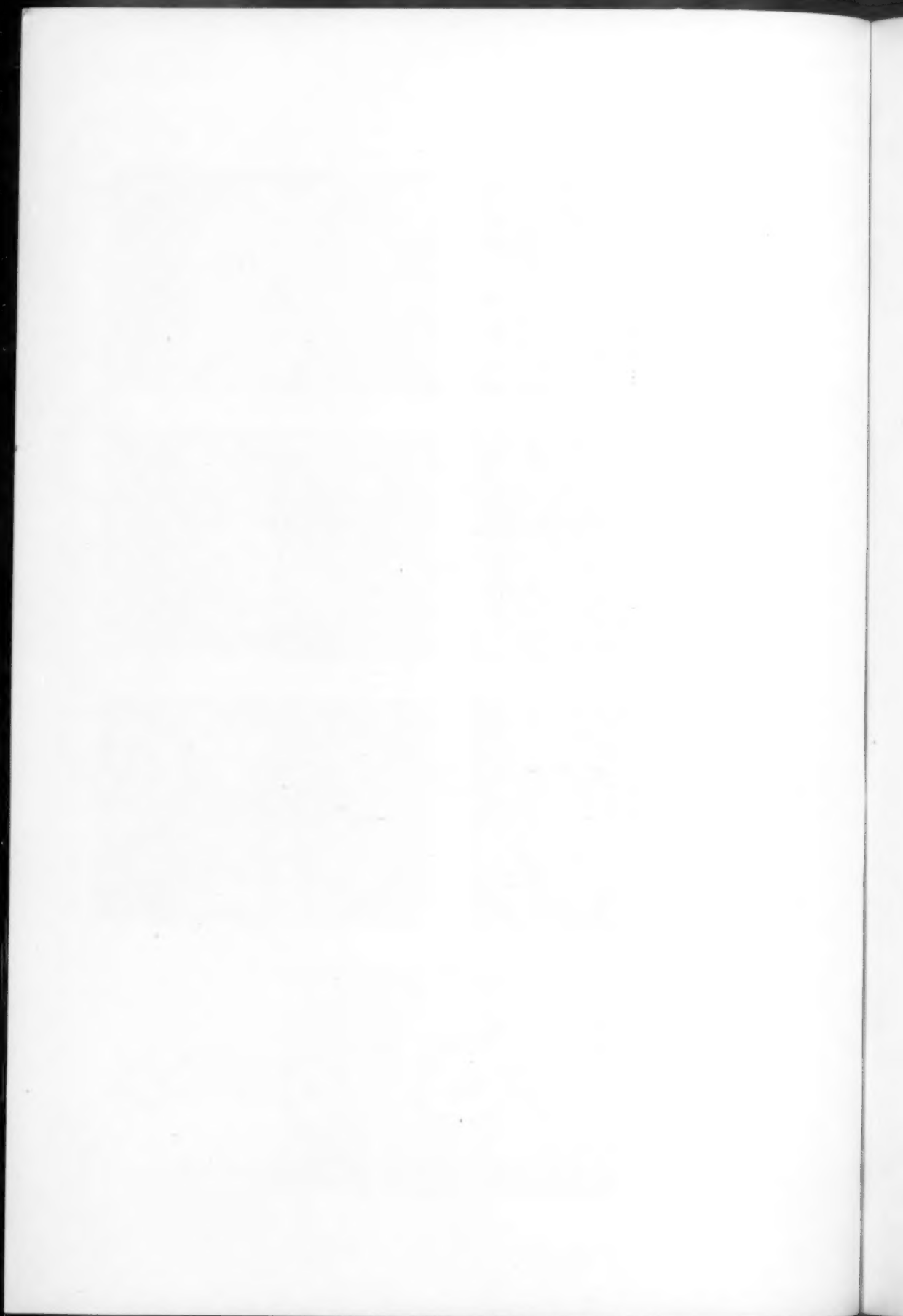
Except for marked pallor the physical findings were within normal limits on admission. The hemoglobin was 6 Gm., and the red blood cells 2,760,000. The leukocyte count was 6,100, with 48 per cent polymorphonuclear cells, 50 per cent lymphocytes and 2 per cent monocytes. The platelet count, the bleeding and coagulation times were normal. The stools were tarry and gave a 4-plus reaction to the guaiac test. No abnormalities were found on proctoscopic examination. He was given small transfusions of whole blood in preparation for surgery.

*Operation.*—On the 5th hospital day, celiotomy was performed under ether anesthesia. The preoperative diagnosis was Meckel's diverticulum, with ulceration and hemorrhage.
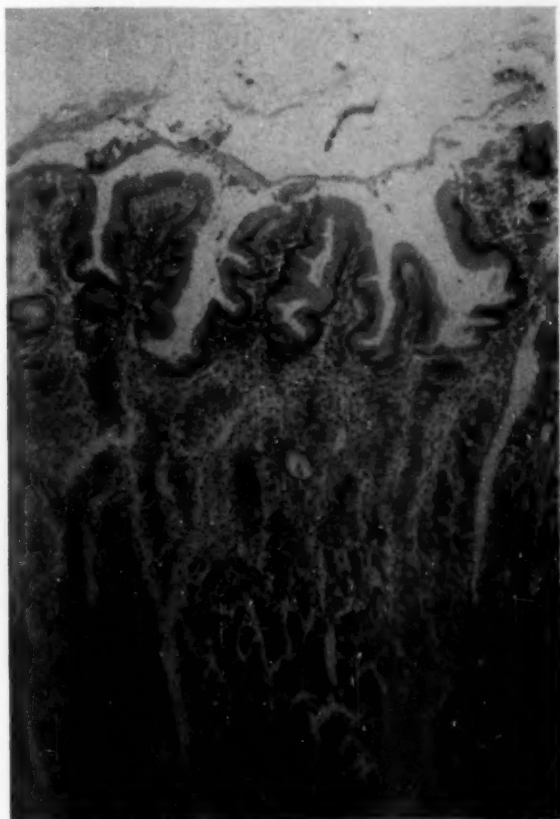


Fig. 1.—Case 1: Hyperplastic gastric mucosa lining
the duplication.

About 20 cm. proximal to the ileocecal area a duplication of the bowel was found (Plate IC). Starting at the distal end and following it backward, we found that the duplicate intestine was attached to the ileum and coursed proximally along its mesenteric side for 10 cm. It then deviated from the normal bowel and continued separately for a total distance of 22 cm., cephalad and posteriorly, along the mesentery to the region of the pancreas. After its separation from the normal bowel, the duplication resembled small intestine for about 10 cm. A dilated segment was then met, measuring 6 cm. in length. This portion contained blood and an ulcer was palpable on the posterior wall. Beyond this there was a narrow empty segment, 2.5 cm. in length, followed by a rounded enlargement, 1.5 cm. in diameter. There then was another narrow segment, 1 cm.

in length, and the final portion, or the proximal extremity of the duplication, was a slightly enlarged blind end about 1 cm. in diameter.

Dissection was started at the proximal or free end of the duplication and mobilization was possible without interfering with the blood supply to the normal bowel. This was carried out down to the point where the accessory intestine fused with the normal ileum. Here, the mesenteric vessels were common to both duplication and normal bowel. This part of the anomaly was then resected together with the contiguous normal ileum and a side-to-side anastomosis performed. Convalescence was uneventful, and the patient was discharged on the 14th postoperative day.

Follow-up.—When last seen, November 22, 1946, 11 months after operation, he was developing normally, his nutrition was excellent and there were no symptoms referable to the alimentary tract.



FIG. 2.—Case 2: Section through the chronic ulcer in the dilated middle portion of the duplication. The margin of the ulcer is formed by ileum. Gastric mucosa, which is not shown, is nearby.

Pathology.—The gross external findings were essentially the same as described in the operative note above. On section (Plate IC), the orifice by which the duplication communicated with the ileum was found at the lower (distal) end of the accessory intestine. The mucosa of the lower portion of the duplicate bowel (that part which paralleled the normal ileum and extended to the dilated segment) resembled jejunum and the lumen contained thin watery fecal material. The mucosa of the dilated midportion was thick, and resembled gastric mucosa. It bore a rather deep ulcer, 1.5 cm. in diameter, with thickened margins and a bed of fibrous tissue. The mucosa of the two rounded enlargements at the upper end was thick and infolded, and also resembled gastric mucosa. The mucosa of the two narrow areas was thin and smooth.

Microscopically, one section through the lower or distal half of the duplication showed mucosa resembling that of the colon and bore a small ulcer extending into the submucosa. A second section through the lower end of the duplication showed gastric mucosa.

A section through the ulcer in the dilated part of the accessory bowel (Fig. 2) showed small intestinal mucosa on both sides of the ulcer. On one side, however, slightly beyond the intestinal mucosa, there was an abrupt transition to well-differentiated gastric

mucosa. The ulcer extended to the level of the muscularis, and beneath this there was a thick wall of fibrous tissue containing many fibroblasts and young fibrocytes. The underlying peritoneum was thickened with fibrous tissue and covered with a delicate layer of fibrin. A few lymphocytes, plasma cells and phagocytes infiltrated the entire scarred area, and there was fresh hemorrhage into the deeper portion.

Sections through both nodular enlargements of the free end of the duplication showed gastric mucosa infiltrated with a few eosinophils.

A section through the narrow segment connecting the two nodular enlargements was



Fig. 3.—Case 2: Section through the narrow por-
tion near the free end of the duplication in which the
mucosa resembles that lining the common bile duct.

lined with a thin and irregular layer of high columnar cells which suggested the struc-
ture of common bile duct mucosa (Fig. 3).

The mucosa of the resected normal small intestine was edematous and bore transverse folds as in jejunum. A few Paneth cells were present and also a cluster of three lymph follicles. It was not clear whether the mucosa was that of jejunum or ileum.

Case 3.—J. H., a five-year-old white boy, was admitted to Babies Hospital, February 25, 1946, because of abdominal pain and vomiting of six days' duration. The pain was intermittent and confined to the lower abdomen. Vomiting followed the onset of pain and had occurred about twice daily. The stools were normal until the day of admission, when they became liquid, and contained some small blood clots.

On admission, the physical findings were within normal limits except for minimal tenderness and rigidity over the right lower quadrant of the abdomen. The temperature was 100.4 F., pulse 88, respirations 22. The leukocyte count was 18,400, with 77 per cent polymorphonuclear cells and 23 per cent lymphocytes. The red blood count and urine analysis were normal. The sedimentation rate was 19 mm. in one hour. The stools gave a 4-plus reaction to the guaiac test. No pathogens were recovered from stool culture. The Kline test was negative.

The next day, the leukocyte count was 10,600, with 68 per cent polymorphonuclear cells and 32 per cent lymphocytes. Physical findings were the same. On the 4th hospital day, roentgen study of the colon by means of a barium enema disclosed no abnormality. The patient remained asymptomatic for the next three days.

On the 7th hospital day, shortly after breakfast, he suddenly complained of lower abdominal pain. He was not nauseated, and did not vomit. There was moderate tenderness over the lower abdomen, slightly more on the right than the left, but no rigidity. Rectal examination was normal. He had a normal bowel movement one hour later. The temperature was normal. The leukocyte count was 16,200, with 88 per cent polymorphonuclear cells. By the afternoon, eight hours after the onset of pain, he was asymptomatic and physical findings were normal. The next day, the leukocyte count was 10,000, with 65 per cent polymorphonuclear cells. Two days after this episode, he was again seized with severe pain in the left upper quadrant, which soon shifted to the lower abdomen, and was accompanied by nausea and vomiting. At this time, there was marked tenderness and rigidity of the entire lower abdomen.

*Operation.*—Celiotomy was performed, and a small duplication of the ileum was found 30 cm. proximal to the ileocecal area. It measured 3 x 2 x 2 cm., and extended out between the leaves of the mesentery. (We do not have a photograph of this specimen but it closely resembled that found in Case 1 (Plate IA). About 200 cc. of serosanguineous fluid were present in the peritoneal cavity. The terminal ileum was edematous and thickened. The duplication and about 10 cm. of ileum above and below it were "peppered" with areas of subserosal hemorrhage. The mesentery and its nodes in this region were thickened and edematous. It seemed probable that the duplication had produced an intussusception, which had reduced spontaneously just before operation. In all, 24 cm. of the ileum together with the duplication were resected and a primary anastomosis performed. Convalescence was uneventful, and the patient was discharged on the 10th postoperative day.

*Follow-up.*—This patient was last seen on November 22, 1946, nine months after operation, when he was asymptomatic.

*Pathology.*—The gross external findings were as described above. In a section through the duplication, the mucosa showed transverse folds and resembled duodenum. The mucosa and part of the submucosa were densely packed with polymorphonuclear cells, phagocytes and red blood cells. Some of the superficial portions of the villi had lost their epithelium. Most of the muscle cells showed early necrosis. The peritoneum was hemorrhagic. The section suggested early gangrene. A section through the adjacent ileum showed edema and infiltration of the mucosa with polymorphonuclear cells. Sections taken farther away from the duplication were normal.

**Case 4.**—B. M., a ten-months-old white male, was admitted to Babies Hospital, February 22, 1946, with a fistula in the right upper abdominal quadrant. At the age of three weeks this patient was said to have a small, red, tender mass in the right upper quadrant. Two months later, when the mass had increased to the "size of a plum," he was admitted to another hospital where a diagnosis of abdominal wall abscess was made. The mass was incised but no pus was found; only "edema and thickening of the abdominal wall." Two weeks later he was admitted to the same hospital with the same mass and a fistula at the site of incision. The fistulous tract was excised. One week after this operation, "intestinal fluid" began to drain from the incision, which failed to heal. Four months later, another unsuccessful attempt was made to excise the fistula, and the wound

continued to drain. He received nine blood transfusions during his period of hospitalization. Roentgenographic studies of the gastro-intestinal tract, both with barium meal and barium enema, were reported to be normal, as was also an intravenous pyelogram. At the age of ten months, the patient was transferred to Babies Hospital.

On admission, examination revealed a very alert, marasmic infant, who was in no acute distress (Fig. 4). The abdomen was distended but soft and presented a large



FIG. 4.—Case 4: Photograph on admission. A dressing soaked with sodium bicarbonate solution is seen in the large fistula.

fistula in the right upper quadrant. The ulceration was about 4 cm. in diameter and about 2 cm. in its deepest portion. It was surrounded by a large area of excoriation and induration. The fistula drained a copious amount of seromucoid fluid. The red blood count and hemoglobin were normal. The leukocyte count was 19,800, with 54 per cent polymorphonuclear cells. The urine analysis was normal. The serum proteins were 6.05 Gm. per 100 cc., with 4.01 Gm. of albumin and 2.04 Gm. of globulin. The plasma chloride

level was 105 milliequivalents per liter. The stools gave a negative reaction to the guaiac test. Roentgenographic studies, with lipiodol injected into the fistula, failed to demonstrate any connection with the alimentary tract. Visualization of the gastro-intestinal tract with barium showed the second portion of the duodenum displaced to the left, suggesting a mass impinging on its descending limb from the right. There was no evidence of obstruction.

Methylene blue fed by mouth failed to appear in the fistula. In an histamine test, the fluid flowing from the fistula was collected quantitatively, as if for gastric analysis, with the following results: The free HCl before histamine was zero; the total acidity 70. After histamine, the free HCl was 38.5; the total acidity 79, and the amount of drainage was considerably increased. By direct measurement, the pH of this fluid was 3.0. Pancreatic enzyme assay performed on the fluid showed no trypsin or amylase. The fistulous tract was continuously treated with dressings of sodium bicarbonate solution, and the surrounding skin slowly began to improve. The discharge was so irritating to the skin that at one time, when the dressings were neglected overnight, a red tract of excoriated skin was seen the next morning where the fluid had run down the flank.

After four weeks of supportive therapy the skin around the fistula had improved sufficiently to permit operation. From the evidence gathered, we expected to find a duplication of the stomach, probably devoid of direct communication with the alimentary tract.

*Operation.*—Celiotomy was performed, under ether anesthesia, March 26, 1946. The patient received 200 cc. of whole blood during the procedure. A subcostal incision, just above the fistula, was made. Because of the dense adhesions encountered, the lateral end of the incision was extended downward and medially below the fistula in order to secure adequate exposure. The fistulous tract led into a cystic mass which was round, thick-walled, and grossly resembled stomach. The mass lay in the gastrohepatic omentum and was in contact with the edge of the liver and fundus of the gallbladder anteriorly and the transverse colon posteriorly and inferiorly. The stomach was normal. A loop of jejunum was adherent to the point where the fistulous tract joined this mass and communicated with the tract through a minute opening. This was interpreted as a traumatic fistula probably resulting from one of the previous operations. The mass itself, however, had no direct communication with any of the viscera.

The adherent loop of jejunum was dissected free of the fistulous tract and the small opening in it was closed. The duplication was then dissected free from the surrounding structures and was removed together with the fistulous tract. The incision was closed in layers, and the fistulous opening remaining in the abdominal wall was packed with gauze.

This opening soon filled-in with granulation tissue and became covered with epithelium. A small segment of skin in the lower extension of the incision sloughed because of poor blood supply, and this defect was allowed to heal by granulation.

Six weeks postoperatively the patient developed mumps, and was transferred to the Willard Parker Hospital. He was readmitted to Babies Hospital one week later for further care of his wound. He was discharged on June 15, 1946, when the wound was entirely healed.

*Follow-up.*—He was last seen, October 25, 1946, seven months after operation. He had gained a great deal of weight and was developing normally. There were no symptoms referable to the gastro-intestinal tract. The wound was well-healed but presented some weakness at the lateral end of the subcostal scar.

*Pathology.*—The specimen (Plate ID) consisted of a rounded mass measuring 3.3 x 2.8 x 2.2 cm. It bore two short projections: one measured 1 cm. in diameter and 0.5 cm. in length and was patent; the other was a tag of fibrous tissue 1 cm. in length. On section, the cystic mass contained 5 cc. of thick, cloudy, brownish-black fluid. The inner surface resembled gastric mucosa. No ulcers were seen. The wall measured 5–6 mm. and was formed of a mucosal and a muscular layer of about equal thickness.

The microscopic sections resembled hyperplastic stomach wall. The mucosa was thick and the chief cells were clearly seen. No ulcer was present. The muscularis was in two layers with distinct sympathetic ganglia between them. The muscle fibers were hypertrophied. The peritoneum was somewhat edematous.

Case 5.—J. B., a three-months-old white male, was admitted to Babies Hospital, May 7, 1946, because of bleeding per rectum. The baby was well until three weeks previously, when the mother noted fresh blood on his diaper. The next day he passed blood clots by rectum, following which he began to look pale. The hemoglobin was reported to be 40 per cent, and he was admitted to another hospital for transfusions and surgery. At operation, a duplication of the ileum was found. No resection was attempted because of his poor condition. In the first days after exploration, he had eight bloody stools, received two blood transfusions, and then gradually began to show improvement. Two weeks after operation he had an "alarming rectal hemorrhage," was given another transfusion of whole blood and transferred to Babies Hospital.

On admission, the infant was very pale and listless. The abdomen was soft and showed a healed right rectus incision. No masses were palpable. Gross blood was found in the rectum on digital examination. The hemoglobin was 9 Gm., the red blood cells 3,700,000. The leukocyte count was 16,000, with 45 per cent polymorphonuclear cells and 55 per cent lymphocytes.

After a transfusion of 100 cc. of whole blood the hemoglobin rose to 11.7 Gm. and the red blood cells to 4,300,000. He continued to pass small quantities of gross blood by rectum.

*Operation.*—On the 3rd hospital day operation was performed under ether anesthesia. About 25 cm. proximal to the ileocecal region, a duplication was found which measured 15 cm. in length (Plate IE). The duplication and the contiguous ileum were resected.

Convalescence was uneventful and the patient was discharged on the 13th postoperative day.

*Follow-up.*—He was last seen, November 26, 1946, six months after operation; he was asymptomatic, and no further bleeding had been observed.

*Pathology.*—The specimen (Plate IE) consisted of a segment of ileum measuring 20.5 cm. in length and 1.3–1.5 cm. in diameter. Running parallel to it, on the mesenteric side, and enclosed in the same peritoneal sheath, there was a duplicate segment of intestine measuring 15.5 cm. in length and 1.8–2.2 cm. in diameter. The junction of the two, near the distal end of the specimen, extended for a distance of about 3 cm. The mucosal surface of the ileum looked normal except for the presence of the orifice into the accessory intestine. This appeared as a transverse slit 1.2 cm. in width. The mucosa of the duplication was thick and somewhat irregular, resembling that of the stomach. The transition to ileal mucosa was abrupt and followed a transverse line just proximal to the communication.

Microscopically, the sections showed a portion of ileum which made an abrupt transition to hypertrophic gastric wall. The gastric mucosa was very much infolded. The deeper layer contained normal gastric glands with numerous chief cells. The stroma was infiltrated with a moderate number of lymphocytes. The muscularis was normal and the peritoneum was thick and edematous.

Case 6.—R. N., a six-year-old white boy, was last admitted to Babies Hospital, November 10, 1946, with a history of abdominal pain and bleeding per rectum. His illness began at the age of three months, when the parents first noticed that his stools were tarry. This condition was only temporary. When he was seven months old he passed two large bloody stools for which he was admitted to another hospital and received two blood transfusions. Roentgenographic studies were made of the gastrointestinal tract, including barium enema. These were reported to be normal and he was discharged after eight weeks of observation.

He was first admitted to Babies Hospital in 1942, at the age of 15 months, because he had again passed gross blood by rectum. The hemoglobin was 5.1 Gm. (35 per cent),

and the red blood cells 2,200,000. He received two transfusions. Proctoscopic examination did not reveal any abnormality.

On the 10th hospital day celiotomy was performed. The preoperative diagnosis was Meckel's diverticulum, with hemorrhage. A duplication of the distal ileum was found which was estimated to be 24 inches long. There was an inflammatory mass in the midportion of the lower abdomen involving the tip of the appendix, the proximal end of the duplication and a loop of ileum. There was a fistula between this loop of ileum and the duplication. The adherent loop of ileum was dissected free of the mass and the openings in this loop and in the duplication were closed. The appendix was mobilized and removed. Three ulcers were palpated in the duplication. Since the condition of the patient did not justify an extensive resection, the ulcers were inverted with purse-string sutures and the abdomen closed. Convalescence was uneventful. He was discharged, and was to return at a later date for resection of the lesion.

Two months later, at the age of 17 months, he was readmitted because of intermittent abdominal pain and tarry stools. The hemoglobin was 3.8 Gm., and the red blood cells 2,000,000. The parents refused to allow a second operation at this time, and he was discharged after receiving two more blood transfusions.

This patient had seven more admissions to Babies Hospital between the ages of 18 months and four years, each time for abdominal pain, tarry stools and anemia. On each occasion, permission for operation could not be obtained, and he was discharged after receiving transfusions of whole blood. Between the ages of four and six years there were no further episodes of bleeding.

Two days before the most recent admission, he was awakened by severe abdominal pain at 4 A.M., and soon vomited. He ate breakfast at 7 A.M., and vomited again after an attack of violent lower abdominal pain which doubled him up and caused him to roll on the floor. Following this episode, the pain disappeared and the next day fresh blood was noticed in his stools.

Except for marked pallor, the physical findings were within normal limits on admission. The hemoglobin was 5.5 Gm., and the red blood cells 2,320,000. The stools were tarry and gave a 4-plus reaction to the guaiac test. This time permission for operation was granted and he received three transfusions of whole blood in preparation for surgery.

*Operation.*—On the 9th hospital day celiotomy was performed under ether anesthesia. Many adhesions were encountered between the duplication and loops of small intestine. The distal end of the duplication, where it communicated with the normal bowel, was found about 40 cm. proximal to the ileocecal area. It coursed upward along the mesenteric side of the ileum for a total length of 40 cm. (Plate IF). At its proximal extremity it deviated from the normal ileum and ended in a blind pouch between the leaves of the mesentery. The duplicate intestine, together with 60 cm. of the contiguous ileum, were resected.

Postoperatively, he did well except for an episode of abdominal cramps and vomiting on the 8th day which promptly responded to the use of the Miller-Abbott tube. He was discharged on the 20th postoperative day in excellent condition.

*Follow-up.*—This patient was last seen, January 27, 1947, ten weeks after operation. He was having normal bowel movements and there had been no further episodes of pain since discharge. He was gaining weight rapidly, an estimated ten pounds since operation.

*Pathology.*—The specimen (Plate IF) consisted of a loop of small intestine measuring 60 cm. in length and 2 cm. in diameter. A second segment of bowel lay parallel to it on the mesenteric side and within the mesentery, sharing a common blood supply. This measured 40 cm. in length and 2–2.5 cm. in diameter. The duplicate portion communicated freely with the normal intestine at the lower end of the specimen. The proximal end formed a somewhat dilated blind pouch, 4 cm. in diameter. This was demarcated from the remainder of the duplication by a slight constriction 4 cm. from the extremity. The main portion of the duplication measured 5 cm. in circumference. The lumen was filled with dark, brownish-black mucoid material. The mucosa (Plate IG)

was thick and grey, and thrown up into irregular folds, the appearance being that of gastric mucosa. The ulcers described at the previous operation, 4.5 years ago, were not evident. The mucosa of the small intestine was yellowish and bore transverse folds similar to those of the normal jejunum.

Microscopically, the duplication showed normal gastric mucosa diffusely infiltrated with lymphocytes and eosinophils (Fig. 5). No ulcers were present. The submucosa was normal. The circular and longitudinal muscular layers were of approximately equal thickness throughout. They were infiltrated with a few eosinophils. Sections through the contiguous small intestine showed transverse folds similar to those of jejunum. Paneth cells were absent and no Peyer's patches were present. It was not clear whether the mucosa was that of jejunum or ileum.
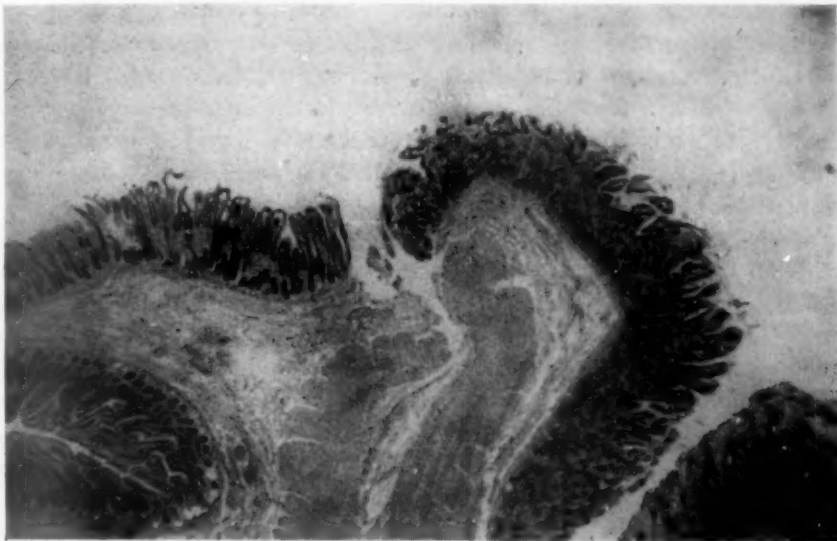


FIG. 5.—Case 6: The section is taken from the junction of the duplication with the intestine. The transition between the gastric and intestinal mucosa is abrupt. The fusion of the muscular coats of the two portions of bowel is demonstrated.

## DISCUSSION

*Embryology.*—There are many theories regarding the origin of duplications. According to Hughes-Jones,[15] the sequestration of embryonal intestinal epithelium early in fetal life may account for the development of these anomalies. Many authors have previously described these cases as representing persistence of the proximal part of the vitelline duct or Meckel's diverticulum. As pointed out by Hudson,[14] the persistence of the vitelline duct, a normal fetal structure, explains many cysts and diverticula but this accounts only for those which occur in relation to the distal portion of the ileum. Also, this theory would not account for the mesenteric position of the duplications as in contrast to the constant antimesenteric location of Meckel's diverticulum. The case reported by Grove and Porch,[12] of a duplication of the terminal ileum associated with a Meckel's diverticulum and an intramesenteric diverticulum in the same patient, would be difficult to explain on this basis.

Probably the most popular theory of their development is that of Lewis and Thyng,[22] who described groups of epithelial cells or diverticular occurring along the alimentary tract of the embryos of the pig, rabbit, cat, sheep and man, which normally disappear. One of these diverticula may be pinched-off and develop into a duplication.

More recently, Bremer[4] divided these anomalies into two groups, the spherical and the tubular, on the basis of embryologic origin. Most of the spherical ones are derived from true diverticula which are frequently found projecting from the antimesenteric surface of the alimentary tube in embryos of the 8th or 9th week. These diverticula normally regress. Abnormally, they continue to grow and give rise to the spherical type of duplication. Most of the tubular structures, and a few of the spherical ones, represent true duplications, originating by an abnormal persistence of the vacuoles which are regularly present in the "solid stage" of the development of the intestine in the 6th or 7th week embryo. By the confluence of a chain of these vacuoles a new channel is formed alongside the original lumen and this develops as a duplication.

*Pathology.*—Duplications may occur anywhere along the gastro-intestinal tract, from the base of the tongue to the rectum. They are most commonly found along the ileum: seven out of the 18 cases reported by Ladd and Gross,[20] five of our six. These lesions may also be found in the mediastinum, as reported by Mixter and Clifford,[24] and others.

The duplicate intestine is usually intimately associated with the normal adjacent bowel, lying on its mesenteric side, between the leaves of the mesentery. The blood supply of the duplication and that of the contiguous intestine are the same. This is of primary importance in the surgical management of these lesions and will be given greater consideration later. Rarely, the malformation may be entirely separate from the alimentary tract, as in one of our cases (Case 4), and is then commonly referred to as an enteric or enterogenous cyst.

These structures may be spherical or tubular. They may vary considerably in size; from 2 cm. to 40 cm. in our cases. Hudson[14] reported one of the ileum about four feet long. They may be multiple, as in the case reported by Poncher and Milles.[26]

The duplication may communicate with the adjacent intestine at one or more points, or not at all. Only two of the 18 cases reported by Ladd and Gross[20] had such an opening. Five of our six cases communicated with the normal bowel. From a study of our cases and a partial survey of the literature, it seems that in the elongated type the duplication usually communicates with the contiguous normal intestine near its distal portion and ends blindly in the mesentery in its proximal portion.

The structure of the duplication is essentially that of the gastro-intestinal tract; the wall being made up of mucosa, smooth muscle and serosa. The mucous membrane is not necessarily the same as that of the adjacent segment of intestine. In three of our cases it was entirely gastric, in one it was gastric

and small intestinal, in one it was duodenal and in one it was mixed, containing gastric, small intestinal, colonic and common bile duct mucosa.

The occurrence of ectopic gastric mucosa is often associated with ulcers and bleeding. However, bleeding may occur with apparently intact mucous membrane (Cases 5 and 6). Acute perforation has been reported by Black and Benjamin.[3] Perforation of an ulcer, with the formation of a fistula into the small intestine, probably occurred early in the disease in one of our cases (Case 6).

It is curious that in two of our cases (Cases 2 and 6), the resected normal intestine resembled jejunum more than ileum on pathologic examination although the external appearance and relations, as seen at operation, were definitely those of ileum. We have no explanation for this observation nor have we found any reference to it in the literature.

*Clinical Findings.*—The incidence of this condition is difficult to determine. Certainly, it is rare. The fact that we operated upon six cases in a period of 18 months, and that they are being more frequently reported by others, leads us to believe that these abnormalities may not be as rare as previously supposed.

Duplications are usually found in infancy and childhood, but they have been reported in older patients.[5, 9, 23] Our youngest patient was three months old at operation; the oldest was 12 years.

Most of the duplications are found in males, there being only an occasional case reported in females. All of our patients were boys. It is of interest to note that 85 per cent of the reported cases of Meckel's diverticulum are in males,[10] and almost all those associated with bleeding are in the same sex.[1]

There are no characteristic symptoms caused by this anomaly, and a correct diagnosis is rarely made before operation. It may not cause any symptoms and may be discovered as an incidental finding at autopsy. However, it frequently causes serious symptoms. In four of our cases, severe intestinal hemorrhage was the first sign (Table I). Intermittent abdominal pain may be a feature, as in two of the cases. In one of these it was probably due to intussusception of the duplication (Case 3). Palpation of an abdominal mass is a common finding in the series reported by Ladd and Gross.[20] One of our most unusual cases (Case 4) presented a fistula which followed incision of a palpable abdominal mass at another hospital. In none of our other cases was the duplication palpated preoperatively. The anomaly may lead to intestinal obstruction by encroaching on the adjacent bowel, by taking part in a volvulus as in one of Hudson's[14] cases, or by forming the leading point of an intussusception, as in a case reported by Ladd and Gross,[20] and one presented by Kimpton and Crane.[16] There may be severe anemia in the bleeding cases. Malnutrition may be an important part of the picture in some instances.

Roentgenologic findings are not characteristic. The diagnosis is only rarely suggested by displacement of the normal bowel by an abnormally situated air-containing viscus. The duplication is not outlined by barium.

In the differential diagnosis, Meckel's diverticulum, intestinal polypus,

mesenteric cyst, urogenital cyst, dermoid or teratoma, hydatid cysts and pancreatic cysts are to be considered. Meckel's diverticulum with hemorrhage was the preoperative diagnosis in four of our cases. With this experience, we now think of duplication as frequently as we do of Meckel's diverticulum in cases of intestinal hemorrhage.

*Treatment.*—The treatment in all instances is surgical and should consist of resection or excision of the anomaly. In the majority of cases, the duplication is intimately attached to the contiguous bowel and separation is impossible without entering the lumen. Furthermore, the blood supply is usually common to both the duplication and the adjacent intestine. The malformation lies between the leaves of the mesentery with the mesenteric vessels coursing over it, anteriorly and posteriorly, and then supplying the contiguous normal bowel distally. For these reasons, resection of the duplication alone is usually impossible and resection of the adjacent bowel is also necessary. This was done in five of our cases. Rarely, the duplication is entirely separate from the alimentary tract and may be excised alone without compromising the blood supply to adjacent structures. This was accomplished in one of our cases.

TABLE I

DUPLICATIONS OF THE ALIMENTARY TRACT*

| No. | Age | Presenting Symptoms | Location and Size | Type of Mucosa | Treatment |
|-----|-----|---------------------|-------------------|----------------|-----------|
| 1. | 12 yrs. | Bleeding | Terminal ileum 3 x 2 x 2 cm. | Gastric and small intestinal | Resection and anastomosis |
| 2. | 3 mos. | Bleeding | Terminal ileum 32 cm. long | Gastric, colonic, common bile duct, small intestinal (jejunal?) | Resection and anastomosis |
| 3. | 5 yrs. | Pain and bleeding | Terminal ileum 3 x 2 x 2 cm. | Duodenal | Resection and anastomosis |
| 4. | 10 mos. | Mass and fistula | Gastrohepatic omentum 3.3 cm. in diam. | Gastric | Excision |
| 5. | 3 mos. | Bleeding | Terminal ileum 15.5 cm. long | Gastric | Resection and anastomosis |
| 6. | 6 yrs. | Bleeding and pain | Terminal ileum 40 cm. long | Gastric | Resection and anastomosis |

* Table of Cases listed in their chronologic order of operation, and corresponding to the Case numbers in the text.

All patients made an excellent recovery.

Operations of lesser magnitude, such as marsupialization of the duplication, with subsequent destruction of its mucosa, or the procedure presented by Gardner and Hart[11] of creating a window between the anomaly and the adjacent bowel, may be necessary because of the poor condition of the patient or the location of the anomaly.

### SUMMARY

1. Six cases of duplication of the alimentary tract are presented. Successful resection of the anomaly together with the contiguous intestine was accomplished in five and excision was performed in one.

2. The condition is more commonly seen in infancy and childhood than in the older age-group, and more commonly in males than in females.

3. It is suggested that duplications of the alimentary tract are not as rare as previously supposed and should always be considered in the differential diagnosis of massive intestinal hemorrhage in the younger age-group. Four of our cases presented severe hemorrhage as the first symptom.

4. With proper preoperative management, resection or excision of these anomalies can be performed with complete relief of symptoms.

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# A PSYCHIATRIC STUDY OF SIXTY-ONE APPENDICECTOMY CASES*

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SURGEONS, and the medical profession generally, have long realized that emotional disturbances of varying depth and intensity may accompany disorders requiring surgery. Marked anxieties, hysteria, and a whole catalog of neurotic manifestations are commonly encountered, both preoperatively and to a lesser extent, postoperatively. Until quite recently, however, the nature and origins of these emotional disturbances were not fully appreciated. They were either completely neglected, or regarded merely as natural by-products of a surgical experience admittedly harrowing to the patient.

In January, 1943, the Department of Surgery of Vanderbilt University Medical School, with a view to widening the borders of knowledge in this field, began a study of certain surgical problems where the emotions seemed to play a rôle. The purpose of this study was to discover, clinically, how the emotions enter into the etiology, treatment and convalescence of surgical patients and to determine how psychiatry can aid the surgeon in curing the patient. Implicit is the assumption that every sick person has a psychologic as well as a somatic aspect to his illness.

This paper is based on the study of 61 consecutive admissions of patients operated upon for appendicitis.

## DESCRIPTION OF PATIENTS

Our patients were white men and women, all between the ages of 16 and 55, from the Middle Tennessee hill section. They showed a wide variation in schooling and intelligence. The fact that most of these patients, and their parents before them, were more or less permanent in their residence made it easier to get complete family histories and to carry on follow-up studies.

The majority of the Middle Tennessee hill people are of Scotch-English descent; their native reserve and emotional control is somewhat comparable to that of the American Indian. Whatever attitudes of fear, anxiety and grief that the patients might hold, they usually appeared calm and unperturbed. Occasionally their reserve was so great as to be virtually impenetrable. Nevertheless, since the authors have lived in this section, our rapport with patients was usually sufficient to enable us to detect their emotional motivations, allay

much of their preoperative worry and help in doing away with postoperative anxiety.

<div align="center">PROCEDURE</div>

We could only occasionally make preoperative psychologic studies, since most of the patients were operated upon as soon as possible after a diagnosis of appendicitis had been made. Usually, though, we could see the patient briefly before operation and observe him for signs of anxiety. For the most part, we were able to take some steps toward relieving this anxiety and make the patient's adjustment to the operation easier.

Then, about 12 hours after the operation, systematic psychologic studies were begun. We secured personal and family histories from the patients and their relatives. These histories brought out many details which bore directly or indirectly upon the understanding of patients' emotional adjustment.

The use of the Wechsler-Bellevue and Stanford-Binet intelligence tests, not only gave us the level of the patient's general intelligence but also told us much about his patterns of belief and his reactions to failure, success, praise, fatigue and illness. The reactions of the patients to test material gave evidence of the presence or absence of anxiety; if anxiety was present, we had to decide whether it was temporary or associated with some basic personality picture.

We also made consistent use of the Rorschach method to gain a knowledge of the patient's basic personality trends and deviations which were, in turn, leads for further clinical investigation.

After all psychologic studies were finished and the case history as complete as possible, we studied the data and then began psychiatric interviews with the patient. Often these interviews lasted over several weeks. We encouraged the patient to talk about his home, his relationships toward his family and friends, his work or school experiences—anything in his life which might have a bearing on his attitude toward the illness. We discussed the patient's dreams, moods and thoughts. We had the patient describe his anxieties before the operation, his attitude toward the anesthesia and anxieties after the operation. We carried on a sort of modified mental analysis, by which we were generally able to resolve many of the patient's worries and help him through his convalescence. Naturally, if anxiety is aroused, one factor in the patient's recovery is his ability to handle this anxiety.

We also obtained the surgeon's views on the patient's physical condition and emotional attitudes. The observations of the psychiatrist, the psychologist and the surgeon were all taken into consideration. This combination provided a basis for coming to grips with the problem of anxiety and its relation to the experience of an appendicitis operation.

<div align="center">MEANING OF THE OPERATION</div>

The present-day attitude of the public toward surgery has an important bearing on the attitude of the individual patient. As recently as 20 years ago, people felt that when a person was taken to the hospital to be cut open he was

as good as dead. Today, the public, even in these backward hill sections, has confidence in the surgeon. Conscious anxiety over the outcome of an operation is materially lessened, and the individual patient facing a surgical operation has little fear that death will result.

Anxiety remains, however, in the *unconscious mind*. In his unconsciousness, the patient sees the surgical operation as an attack upon his safety, which is to result in a grievous wound upon his body. To consent to such a thing the patient must reach a stage of complete acceptance. He will have to put himself entirely in the hands of the surgeon, and when general anesthesia is used, he will have to be willing to allow himself to be made unconscious. Even though his conscious mind may see the necessity of the course, the unconscious mind often cannot achieve the passivity necessary to accept such a death-like state without some fear and opposition.

To counterbalance this, however, other attitudes influence the degree of this fear and opposition. For instance: An operation is an exciting event in the life of a person whose emotional outlook is limited; it is a dramatic episode that gives temporary surcease from the hard work and dullness of a life of poverty; it necessitates attention and care. Often such considerations are so strong that the patient welcomes the operation. Again, a certain type of neurotic patient may welcome an operation because, to the unconscious mind, it represents a physical punishment. Such patients have carried over from childhood a deep-seated sense of guilt for some real or fancied sin. So, to the unconscious mind, the operation is a means of atonement.

To atone for such a sin, a certain kind of neurotic patient has an unconscious wish to be emasculated. To such a patient removal of the appendix is a symbol of emasculation and results in a feeling of satisfaction. To some neurotic women the appendicectomy represents an abortion or a delivery. It, therefore, fulfills an unconscious wish.

Most people realize that the appendix is a useless organ which may, without notice, cause them illness. Therefore, when the pain and inconvenience are over, the average person is glad to be rid of such a potential threat of disease. All too frequently, however, the patient's attitude is markedly neurotic, characterized by intense fear, depression, anxiety and hysterical symptoms. During our psychiatric interviews with the 61 patients, we endeavored to find the basis for these attitudes. Then we went about reorienting the patients by giving them some insight into their problems.

### RATINGS

For this study we classified the patients according to their degrees of anxiety, rating them as A, B, C, D and E (Table I). The anxiety of patients in the first three ratings is considered non-neurotic. The last two ratings are in the neurotic range.

In Rating A falls the patient with no particular anxiety. Such patients thought of little besides their severe pain, and the operation, even though it

might otherwise have held some dread, was welcomed as a release from the pain. Twenty-three per cent fell in this group.

In Rating B are those who showed a certain amount of anxiety before the operation, as evidenced by their anxious facies, vasomotor instability, over-talkativeness, *etc.* These patients reacted very well postoperatively and regained their physical and mental equilibrium with ease. Fifteen per cent fell in this group.

A third group of patients, in Rating C, has a considerable amount of *repressed* anxiety when relieved from the severe pain which they were suffering. Part of this was derived from a definite cultural pattern, since these Tennessee hill people habitually repress emotional expression. Thirteen per cent fell in this group.

TABLE I

PATIENTS BY RATINGS

|  | Number of Patients | Per Cent of Patients |
|---|---|---|
| Non-neurotic: | | |
| (A) No marked anxiety | 14 | 23% |
| (B) Preoperative anxiety with postoperative relief | 9 | 15% |
| (C) Repressed anxiety, with welcome relief from pain | 8 | 13% |
| Neurotic: | | |
| (D) Hysterical reaction (anxiety hysteria) | 11 | 18% |
| (E) Marked anxiety aroused, not relieved postoperatively (anxiety neurosis) | 19 | 31% |
| Total | 61 | 100% |

Then, in the decidedly neurotic range is Rating D, composed of patients who reacted with an hysterical pattern. Such people often showed marked anxiety and fear. The convalescence of those in this rating depends considerably upon the attitudes of their families and those about them. They were usually emotionally dependent persons, whose hysterical attitudes had been nurtured by their families since early childhood. In this group, too, fall many of the well-known surgical cases where physical symptoms are produced directly by an emotional conflict. In other cases the hysterical reaction is not quite as clear-cut. Sometimes the operation obscures this hysterical reaction for the time being. Thus, it is only after recovery that we can detect the basic hysterical pattern. Eighteen per cent fell in this group.

Finally, in Rating E are a certain number of patients who reacted with marked anxiety. These patients had an anxiety neurosis of long-standing which was heightened by the experience of a surgical operation. Such a patient leaves the hospital with an additional psychologic handicap. The wound heals but the anxiety is increased and the pain often remains. Thirty-one per cent fell in this group.

### DIAGNOSTIC GROUPS

To compare the actual illnesses of these variously reacting patients, their disorders are classified into two groups (Table II). Group I includes the cases of (1) acute appendicitis; and (2) other cases of abdominal disease sufficiently serious to cause an appendicitis-like pain in the right lower quadrant—such disorders as ileitis, ruptured graffian follicles, cystitis, pyelitis, *etc.*

In Group II fall the cases of (1) chronic recurrent appendicitis, so classified when there had been some history of appendicitis attacks but where no acute inflammation of the appendix was found at the time of operation; and (2) undiagnosed disease of the abdomen, so named when neither the surgeon nor the pathologist reported any gross or microscopic lesion in the appendix and where no other pathologic condition of the abdominal organs was found. *All of the patients in Group II, it might be noted, were in the D and E ratings —the neurotic range* (Table III).

TABLE II

PATIENTS BY DIAGNOSTIC GROUPS

| | Number of Patients | Per Cent of Patients |
|---|---|---|
| Group I: | | |
| (1) Acute appendicitis | 36 | 59% |
| (2) Other abdominal disorders | 8 | 13% |
| Subtotal | 44 | 72% |
| Group II: | | |
| (1) Chronic recurrent appendicitis | 4 | 7% |
| (2) Undiagnosed disease of the abdomen | 13 | 21% |
| Subtotal | 17 | 28% |
| Total | 61 | 100% |

### CASE REPORTS

**Case 1.**—An example of Rating A was No. 47, a 17-year-old girl, of good intelligence. Slight and undernourished, she had a very difficult life. Child of separated parents, she worked in a factory eight hours a day and then came home to four or five hours of housework. She had recently had an even more difficult time of it when her sister had been in the hospital with appendicitis. While her mother cared for the sister, the girl had to pay the expenses of her sister's operation out of her own meager wages. Psychologic tests revealed stereotyped, immature responses, but not those of a person with any hysterical mechanism. Her condition was acute appendicitis, and she was suffering so much pain that she welcomed the operation without apparent anxiety. She complained very little, said she was not frightened, and the postoperative course was uncomplicated.

COMMENT: Apparently to this patient the operation meant a relief from her hard, ugly, everyday life. It meant good care and attention with a welcomed release from pain. Her attitude toward surgery was entirely non-neurotic.

**Case 2.**—Rating B is well illustrated by No. 58  This patient showed a great deal of anxiety before the operation; knowing something of the circumstances of her life we could have mistaken her illness for an hysterical mechanism to escape marriage. The facts were, however, that she and her fiance had consummated their marriage the week before and were to have been married on the day of her operation. Feeling that she was already married in all but name the patient had the feeling of being torn from matrimony and this was the apparent cause of her worry. She was a spoiled only child, quite stubborn and negative. Her medical history showed several previous attacks of appendicitis, but she had refused to have the operation performed until the condition became acute and the appendix was ruptured. After the operation the patient made a rapid recovery.

COMMENT: Though the effect of the operation had been to arouse anxiety, this patient had the resources to regain emotional equilibrium quickly. She was very proud of the successful way she came through the ordeal.

TABLE III

PATIENTS BY RATINGS AND DIAGNOSTIC GROUPS

| Ratings | Group I (Appendicitis) | | Group II (Not appendicitis) | |
|---|---|---|---|---|
| | No. Pts. | Per Cent | No. Pts. | Per Cent |
| Non-neurotic: | | | | |
| (A) | 14 | 32% | 0 | 0% |
| (B) | 9 | 20% | 0 | 0% |
| (C) | 8 | 18% | 0 | 0% |
| Subtotal | 31 | 70% | 0 | 0% |
| Neurotic: | | | | |
| (D) | 0 | 0 | 11 | 65% |
| (E) | 13 | 30% | 6 | 35% |
| Subtotal | 13 | 30% | 17 | 100% |
| Total | 44 | 100% | 17 | 100% |

**Case 3.**—No. 25 was a good example of Rating C, showing a good deal of repressed anxiety but remaining in the non-neurotic range. This was a boy, age 16, reared in a primitive community, suspicious of strangers and new situations. His appendix was found to be gangrenous and perforated and, after the operation, the patient had a difficult time for several days. Psychologic tests showed a great amount of anxiety and fear but this was inhibited. One incident illustrated the boy's reserve and suspicion. He lay on his arm for so long that his hand became temporarily paralyzed but he said nothing about it until the condition was accidentally discovered by the psychologist. The patient's dread of the operation was overcome by severe pain, so that he repressed, or blocked-off, his anxiety. During his convalescence he was less sullen, almost cheerful, and after a time said he felt all right and wanted to go home.

We come now to some examples of patients who reacted to surgery in a neurotic way and patients whose neurotic patterns actually gave rise to their physical symptoms.

Case 4.—An interesting example of Rating D (those patients with an hysterical pattern) was No. 12. This was an intelligent Army student who was taking a course in meteorology at Vanderbilt University. Psychiatric interviews showed that he was abnormally attached to his mother and that, as a defense against this, he had turned his affections toward his father. His medical history showed a predilection toward upset stomach and mucous colitis. The vasomotor system showed some instability.

The patient's illness was real enough, with acute pain, tenderness, and nausea. While the surgeons were not sure that he had appendicitis, they considered the fact that he was in the Army and might have an attack at some future time less favorable for operation. Thus, they agreed to operate, and found that the appendix was entirely normal. The boy's attack appears to have been of hysterical origin, abetted by suggestion. Several of his Army friends had had their appendices removed and he had discussed the operation with them. They all agreed that it was a good thing to have the appendix out, because they might have an attack sometime while they were overseas and away from a hospital. (Latent homosexuality, a desire to "be like his buddies," may have been an element here.)

COMMENT: The suggestibility of this patient was a factor in his short and satisfactory convalescence. He accepted psychotherapy readily. We talked over the case with him quite frankly so that he was much better fitted to meet his emotional situation than he was before he came in.

What attitude should the surgeon take toward patients who show symptoms of appendicitis and undergo operations but where there is no disease of the appendix? The Surgical Staff at Vanderbilt University Hospital believe, and we concur with them, that in such cases the facts should be revealed frankly to the patient if his intelligence and emotional make-up permit. The hysterical mechanism should be thoroughly explained to the patient so that he will be able to meet life on a less neurotic basis. If this is not done, the chances are that the pain will return and there will be symptoms which may expose the patient to more surgery.

The soldier patient described above was an intelligent young man, with whom we were able to work effectively. However, more than half of the patients, in whom we found no disease of the appendix, were mentally defective or borderline cases. With persons of such limited intelligence, complete frankness is not desirable since it would only create further anxiety. But even such patients can be helped by suitable psychotherapy.

Case 5.—Also in Rating D was No. 32, a young woman whose illness represented an hysterical attack. She was a woman of dull-normal intelligence, whose hysteria arose from her compelling wish for a child, long frustrated because of her husband's impotence. She had separated from her husband and was living with another man. She pictured the operation in her mind as being the delivery of a child. Her appendix, on removal, was found to be entirely normal. It was a case of phantasy pregnancy, hysterically motivated.

Case 6.—No. 10 illustrates Rating E, including patients with severe anxiety neurosis. This was a 27-year-old woman whose history of weight loss, nervousness, and slightly enlarged thyroid suggested hyperthyroidism. She had acute inflammation of the appendix with gangrene of the distal half. She also had pyelitis on the left side. The patient was very tense and suffered considerably after the operation. On the fourth day she was taken with a deep anxiety about her children at home, and insisted on leaving the hospital to go to them. The children were being adequately cared for by the patient's sister, and there was no need for her anxiety.

Psychiatric interview brought out the fact that she had once induced an abortion. She felt, she said, that she had committed a great sin. She had asked God a thousand times to forgive her. She had never wanted children and was reluctant about having marital relations because of her fear of pregnancy. Our psychiatric interviews showed that she had definite death wishes toward her children and as a result felt a deep guilt. Unconsciously, the operation represented some atonement for sin.

COMMENT: This patient is an example of the bodily punishment attitude some neurotic patients display toward surgery, and one in which we had most gratifying success. We explained to her the basis of her anxiety, and she had some conferences with a minister who is familiar with psychiatry. When she was seen again about three months later, she had gained weight, looked years younger, and seemed to be almost entirely free of her former anxiety.

**Case 7.**—No. 43, a 34-year-old male, from an isolated rural section, who had symptoms of appendicitis, was another case in Rating E, but whose appendix was found to be normal. He was a sexually maladjusted person with a long-standing anxiety neurosis. He complained that his wife "ran around"; he had erotic pictures tattooed on his arms, and he suffered from a feeling of sexual inadequacy coupled with a marked sense of guilt for what he considered sexual transgressions in the past. Psychiatric interviews with this patient brought out the fact that he had an unconscious wish to be castrated in order to atone for his guilt and resolve his sexual maladjustment. He feared castration, also, but the wish was stronger than the fear. His neurosis took the form of an appendicitis attack, but to his unconscious mind the operation connoted emasculation. A month after he left the hospital he said he was "puny" about the legs and hips, and complained of being "no good."

Patients with neurotic patterns do not invariably react to surgery with anxiety, however. Patient No. 17 (Case 7) is an instance in point:

**Case 7.**—No. 17: This patient was an extremely neurotic man, who reacted to surgery without the least anxiety—in fact with great pleasure! He was an hypochondriac who had been coming to the hospital for 20 years with one complaint or another. Pain in the chest, smothering spells, palpitation of the heart, dyspnea and precordial pain, especially pain in the epigastrium, "spreading all over the abdomen" was the way his medical chart read. He was always having trouble with his "stomach." One afternoon he came in with especially severe pain in the lower right quadrant. The intern, knowing his neurotic history, gave him some sedative pills and told him to come back in the morning. In the morning, the examining surgeon ordered the man to the operating room, where it was found that the appendix had ruptured. He remarked, sagely, that appendicitis was a bad thing for a neurotic to have.

Coming out of the anesthetic our patient was a happy man. His attack of honest-to-God appendicitis proved that he had really been sick all those years. "I always knew there was something wrong with me," he exulted. "I always knew there was something there that needed to be cut out with a knife."

A postscript to this case is that after being sent home the patient had a recurrence of the characteristic pain he had before his appendicectomy. He is not yet cured.

### CONCLUSIONS

The surgeon should not be satisfied with only a mechanical operation upon the body which often fails to *get the patient well*. This is true whether the

patient has an acute surgical disease or whether he is showing hysterically originated symptoms simulating a surgical disease. A cure can be best assured when the surgeon-psychiatrist team carries out the following steps:

(1) Preoperative: It is important in every case that the surgeon talk with the patient before the operation, explaining what the operation consists of, the comparative lack of danger, and the procedure following surgery. Where there is a surgeon-psychiatrist team, the psychiatrist can also help in this work. This has a very desirable effect on the patient by reducing his preoperative worry, sometimes almost to zero.

(2) Postoperative: Psychologic studies continuing after the operation will indicate the amount and type of postoperative treatment required. In cases of hysteria where there is no clinical or pathologic abnormality found, it is essential to have some psychotherapy after the operation.

(3) Follow-up: In cases of deep-seated anxiety, it is evident that the patient should have follow-up treatment after he leaves the hospital, with visits by a social worker with psychiatric understanding, and possibly with continued visits to the psychiatrist. Without the follow-up treatment the patient's recovery will not be complete, nor his adjustment adequate.

This article covers only a narrow group of surgical cases—those patients suffering from appendicitis. If it shows that the surgeon needs a psychiatrist-psychologist-social worker-team in this emergency illness, how much more must this be true in chronic cases like tumors, ulcers, cancer, tuberculosis and bone diseases, where the patient's attitude is even more a factor in treatment.

Psychotherapy may not only prevent an unnecessarily prolonged convalescence after necessary operations but may reduce the number of patients having repeated unnecessary operations because of recurrence. For determining the importance of psychotherapy in surgery it seemed best to begin with a study of emotional attitudes of patients before, during and after surgery. This is not so clearly shown in the group of patients selected for this paper but will be demonstrated in other groups of less acute surgical cases studied by the authors, and which will be discussed in subsequent reports.

It was found that these psychiatric studies could be carried on in the wards of the Vanderbilt University Hospital with the full coöperation of the attending staff, residents, interns, nurses and, also, significantly enough, of the patients. We might point out that there was not a single case of objection to the program by a patient, and, in fact, many who were not included in the study felt that they had been neglected. There was not, as some had feared, friction among the staff members in relation to this study.

Most gratifying to all was the fact that the study interfered in no way with the vital relationship between patient and surgeon. This relationship, in conclusion, is as important as anything else in surgical treatment. The psychiatrist calls it emotional transference. In quite simple terms it means the patient's confidence, faith and trust in the doctor. Without this transference—this rapport—the patient's anxiety is likely to be a serious obstacle to smooth recovery. The patient is likely to have more pain before operation, to have

more difficulty with anesthesia, to be less relaxed during the operation, to have more pain afterwards, and to have a longer convalescence. Of course, the older, experienced surgeon knows instinctively the importance of this transference, and acts accordingly. But what we are attempting to do is to help the younger surgeon gain this technic without having to pick it up by years of experience. The presence of the psychiatrist at the surgeon's right hand, far from interfering with this transference, helps to make it more effective.

Of course, where a psychiatrist is not available, it rests with the surgeon to do the whole job of establishing rapport with the patient and dispelling his fears. But in large, busy wards, the psychiatric team is an essential part of the surgeon's staff, if the surgeon's aim is to heal the patient rather than simply to see him recover from an operative wound.

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# LOCAL PENICILLIN THERAPY IN SURGICAL INFECTIONS*

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In a series of 142 patients with surgical infections treated with penicillin, 17 received local penicillin therapy alone, 53 received a combination of local with systemic penicillin therapy, and 72 received only systemic penicillin therapy.

Local penicillin therapy proved equally effective in the treatment of localized areas of infection and in the treatment of accessible localized foci associated with systemic manifestations of infection, particularly when the latter were in poorly vascularized areas or contained much nonviable, necrotic material. Often the well-localized, readily accessible infection could be treated with local penicillin therapy alone. When accessible septic foci and systemic manifestations of infection were combined, local and systemic therapy were effectively given concomitantly. Also, in the prophylaxis of infection in operations in contaminated or infected fields a combination of local with systemic penicillin therapy proved useful. Patients with systemic manifestations of infection or other signs of incomplete localization of infection always received systemic treatment with penicillin.

Wherever it was possible to use local penicillin therapy alone or in combination with systemic penicillin therapy, this treatment appeared to be more effective and more economical than the use of systemic penicillin therapy alone. Often penicillin-sensitive infections were controlled readily with relatively small doses of penicillin in concentrations of only 100 to 200 units per cubic centimeter of physiologic saline. Relatively more resistant strains of organisms, which could not have been reached with the concentrations of penicillin obtainable in the blood stream by systemic therapy, often could be controlled by increasing the concentration of solutions given locally to several thousand units per cubic centimeter. For most local therapy, concentrations of 100 to 500 units of penicillin per cubic centimeter of physiologic saline were used, but often concentrations of 5,000 to 10,000 units and occasionally concentrations of 25,000 units per cubic centimeter were used. The use of high concentrations of penicillin in soft tissue defects apparently caused no harmful effects, but was avoided unless necessary. Concentrations in excess of 1,000 units of penicillin per cubic centimeter of physiologic saline were never used in areas that communicated with the central nervous system or the linings of

serous cavities, unless the infected area was walled-off from the normal tissue by a well-established wall of granulations or pyogenic membrane.

It was necessary to observe very strict aseptic precautions during dressings and injections to avoid the introduction of penicillin-resistant organisms into the area under treatment. The normal processes of autolysis appeared to resolve nonviable débris quickly, once the infection was controlled with local penicillin therapy in small, well localized infected areas, but resolution occurred more rapidly if the débris was removed by some mechanical method, such as aspiration or surgical operation. In larger areas, and particularly in very irregular areas containing numerous ramifications, the use of surgical methods to eliminate nonviable tissue and other débris resulting from infection was found to be necessary.

TABLE I

RECORD OF A PATIENT WITH AN ABSCESS OF THE SCALP FROM HEMATOGENOUS OSTEOMYELITIS OF THE OCCIPITAL SKULL, TREATED WITH ASPIRATIONS OF PUS AND LOCAL INSTILLATIONS OF PENICILLIN SOLUTION (5,000 UNITS PER CC.). FOR INVESTIGATIONAL PURPOSES SYSTEMIC PENICILLIN THERAPY WAS WITHHELD UNTIL THE ABSCESS WAS CONTROLLED WITH LOCAL THERAPY

| Date | Material Aspirated | Penicillin Dosage | Bacteriologic Culture |
|------|-------------------|-------------------|----------------------|
| 9-21-44 | 12 cc. thick yellow pus | 25,000 units | *Hemolytic Staph. aureus* |
| 9-22-44 | 5 cc. hemorrhagic yellow pus | 25,000 units | *Hemolytic Staph. aureus* |
| 9-23-44 | 7 cc. thin hemorrhagic pus | 25,000 units | Sterile |
| 9-24-44 | 5 cc. thin hemorrhagic pus | 25,000 units | Sterile |
| 9-25-44 | 2 cc. thin turbid slightly hemorrhagic pus | 25,000 units | Sterile |
| 9-26-44 | 1.5 cc. thin turbid brownish fluid | 10,000 units | Sterile |
| 9-27-44 | 1.5 cc. thin turbid yellow fluid | 10,000 units | Sterile |
| 9-28-44 | Few drops of thin blood-stained fluid | 2,000 units | Sterile |
| 9-29-44 | 1 cc. thin yellow fluid | 10,000 units | Sterile |

Usually local instillations of penicillin solution once or twice daily sufficed to control, in a few days, infections in walled-off abscesses or in wounds that had been closed. In wounds that were open or partly open, penicillin solutions did not remain in contact with the infected areas long enough to be effective, and it was more desirable to dress the area once or twice daily with an ointment or jelly containing penicillin (usually 500 to 1,000 units of penicillin per Gm.), rather than to attempt frequent dressings or instillations of penicillin solutions. In the presence of penicillin-resistant organisms it was preferable to remove the purulent secretions from the wound and instill penicillin solutions at more frequent intervals, usually three to six hours apart. On two occasions local therapy was given by continuous slow drip infusion (100 units per cubic centimeter of physiologic saline solution), and this method was effective, but cumbersome. In some wounds heavily contaminated with organisms that were markedly resistant to penicillin, other agents had to be used to control the infection.

Effective local penicillin therapy required the services of skilled personnel, and the procedures associated with local treatment with penicillin often consumed much of the time of the attending surgeon. In small, well-localized areas of infection, such as small abscesses, the procedure of aspiration and

local instillation of penicillin solution was applicable (Tables I and II). The skin was prepared by cleansing with a detergent solution. A sterile tray containing two syringes and several sizes of needles was prepared and aseptic precautions were observed throughout the procedure. The penicillin solution was drawn into one syringe, which was temporarily placed aside. With the second syringe and a fine needle, a small procaine wheal was made in the skin at the proposed site of aspiration and the deeper tissues were anesthetized if necessary, then a larger needle (usually No. 18 or 16) was applied to the syringe and introduced into the infected area, and as much of the purulent material as possible was aspirated. The contents of this syringe were used for bacteriologic cultures. The syringe containing the penicillin solution was then fitted to the needle and the abscess cavity partly filled with penicillin solution. The amount of penicillin solution introduced into the abscess cavity usually

TABLE II

RECORD OF A PATIENT WITH A CERVICAL ABSCESS ARISING FROM OSTEOMYELITIS OF THE MANDIBLE TREATED BY ASPIRATION OF PUS AND LOCAL INSTILLATIONS OF PENICILLIN SOLUTION (5,000 UNITS PER CC.). NO SYSTEMIC THERAPY

| Date | Temperature | Material Aspirated | Penicillin Dosage | Bacteriologic Culture |
|---|---|---|---|---|
| 5-2-45 | 102° F. | 38 cc. thick foul grayish pus | 50,000 units | *Anaerobic Staph.* and *Strep.*, *Actinomyces, Bacteroides* and fusiform *Bacilli* |
| 5-3-45 | Normal | 45 cc. more fluid hemorrhagic purulent material | 25,000 units | *Anaerobic Staph.* and *Strep.*, Gram-negative filaments |
| 5-4-45 | Normal | 45 cc. thin hemorrhagic fluid | 50,000 units | *Anaerobic Staph.* and *Strep.*, Gram-negative filaments |
| 5-5-45 | Normal | 20 cc. thin serous fluid | 50,000 units | *Anaerobic Staph.* and *Strep.*, Gram-negative filaments |
| 5-6-45 | Normal | 20 cc. thin serous fluid | 25,000 units | No growth |
| 5-7-45 | Normal | 5 cc. thin yellow serous fluid | 25,000 units | No growth |

was several cubic centimeters less than the amount of pus removed, in order to avoid leakage from the puncture wound after withdrawal of the needle. The site of puncture was sealed with a drop of collodion. Aspirations and injections usually were repeated at 24-hour intervals during the first three or four days of treatment, and after that they were repeated as often as fluid could be obtained.

In infections with penicillin-sensitive organisms the cultures usually became sterile after about 48 hours of local treatment with penicillin. However, it was found to be desirable to continue aspirations and penicillin instillations as long as fluid could be obtained, in order to avoid recurrence of the infection. After two or three treatments the contents of the abscess cavity usually became thin, serous and slightly hemorrhagic in character, and a smaller needle (No. 20 or 22) could be used for the treatments. This closed method of treating small localized infections was valuable because it permitted the penicillin solution to remain in contact with the infected area for long periods, prevented contamination with penicillin-resistant organisms, and often obviated the necessity for surgical incision.

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This method was not suitable for large infected areas, those with ramifications, or those containing considerable amounts of débris that could not be aspirated. In such cases it often was possible to carry out a surgical procedure in which the area was drained through an appropriate incision, all unattached débris carefully removed by irrigation with physiologic salt solution, one or more soft rubber tubes placed in the main cavity and one into each ramification or recess, and the wound closed with a few sutures placed through all layers. The rubber tubes were brought out through a small aperture in the sutured wound or through a small separate incision, and were carefully covered with sterile dressings. Penicillin solution was introduced into the wound through them once or twice daily, the strictest aseptic precautions being used to prevent contamination (with penicillin-resistant organisms). The amount of penicillin solution to be introduced at each instillation was determined at the time of completion of the operation, as it was unnecessary and undesirable to introduce excessive amounts that would serve no useful purpose, and would merely run out of the wound and saturate the dressings. The incisions in these cases were intentionally placed with the object of retaining penicillin solution within the wound (in sharp contrast with the orthodox objective of placing incisions to obtain free dependent drainage). The penicillin tubes usually were removed on about the 7th to 10th postoperative day, and always were withdrawn by the 14th postoperative day. This method proved to be very useful in controlling large and irregular localized areas of infection, prevented secondary contamination with penicillin-resistant organisms, and permitted early healing and restoration of function. However, it must be stated that the outcome of cases treated in this manner depended considerably on the skill and care of the attending surgeon, with particular reference to the thorough completion of the operation and meticulous asepsis in handling the penicillin tubes and dressings postoperatively. All of the patients receiving this type of local penicillin therapy were protected against the possibility of dissemination of infection by preoperative and postoperative systemic penicillin therapy.

Following operations in contaminated areas the wounds often were closed around the ends of soft rubber tubes that had been placed in the depths of the wounds, and penicillin solutions were injected into the wounds through the tubes once daily for seven to 14 days (and rarely longer) postoperatively. Continuous penicillin drip also was used in connection with this method in a few cases. In the group treated by this method some of the wounds containing mixed infections suppurated, but the bacterial flora from such suppuration usually caused only some temporary delay in the healing of the soft parts. This type of treatment was not done at once in wounds containing *Proteus* organisms; instead, the wounds were left open and treated by some other method, and secondary closure was done after *Proteus* organisms had been eliminated. It proved to be much easier to prevent contamination of wounds, by careful aseptic technic during dressings and in handling the tubes during penicillin instillations, than to eliminate the troublesome (but usually not dangerous) penicillin-resistant organisms once they became established. All operations of

this type were preceded and followed by courses of systemic penicillin therapy, in order to avoid the possibility of dissemination of infection.

In cases in which it was necessary or desirable to treat open wounds locally with penicillin, ointments or jellies containing 500 to 1,000 or more units of penicillin per Gm. were used. It was necessary to assay the potency of commercial and laboratory-made penicillin preparations of this type, in order to be certain of their efficacy. In several instances, when effective penicillin preparations were not available, the pharmacist prepared a suitable sterile ointment or jelly base and the surgeon mixed the penicillin solution into the base immediately before applying it to the wound. Open wounds that suppurated considerably required careful cleaning and dressing several times daily. As the wounds became cleaner, the dressings and application of penicillin ointments could be done once daily. This method of treatment was impractical for large open wounds, and it proved to be somewhat laborious, though quite satisfactory and economical, for patients with small open infected wounds in which the predominating pathogen was sensitive to penicillin within the range of potency obtainable in the wound.

Infected serous cavities, such as joints, usually were aspirated and instilled with penicillin solution once daily. For local instillation in serous cavities the concentration of penicillin was usually limited to 1,000 units per cubic centimeter of saline, but higher concentrations could be used in areas where isolated, walled-off abscesses were present. The strictest aseptic technic was maintained in the treatment of infected serous cavities.

In wounds involving the meninges and central nervous system, concentrations of 500 to 1,000 units of penicillin per cubic centimeter of physiologic saline were usually used. All injections of penicillin solution into the subarachnoid spaces were made by lumbar puncture, after first draining all the cerebrospinal fluid that would flow freely. The dose used for intraspinal injection varied from 5,000 to 20,000 units given once or twice daily. Daily bacteriologic cultures were made. The small dose of 5,000 units appeared to be as effective as larger doses of 10,000 to 20,000 units in most infections of the central nervous system. Systemic penicillin therapy also was given in all such cases.

## SUMMARY

Small, well-localized pyogenic abscesses may be treated successfully with aspiration and instillation of penicillin solution. Larger areas of localized infection, especially those with ramifications and those containing much thick, purulent material or necrotic débris, require incision for evacuation. In some of these the incision may be closed at once around tubes through which local penicillin therapy is given; others may require delayed closure. Infections in well-localized areas may be treated with increasing concentrations of penicillin solutions until resistance of the infecting organism is overcome.

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# A SUCCESSFUL METHOD FOR SECURING PRIMARY WOUND HEALING AFTER RESECTION OF FISTULAE IN ANO

A PRELIMINARY REPORT

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THE COMMON AND ACCEPTED METHODS for treating a fistula in ano have always appeared to the author to be archaic and not at all in keeping with modern surgical technic. In fact, they have not appreciably advanced beyond the principles laid down a hundred years or more ago. In the usual procedures described in the literature and in popular textbooks on Surgery and Proctology, the tract is opened widely, destroyed, and the resultant wound then allowed to granulate, that is, heal by second intention. When the tract passes through or under the external sphincter, that muscle is severed by one of several methods, and then nature trusted to unite the cut-ends, something which, to the chagrin of the surgeon, does not always take place. The convalescent period after this type of operation is commonly marked by its length, discomfort, temporary anal incontinence, frequent dressings and sitz baths, and the need for careful and prolonged wound care to insure proper healing. If the cut-ends of the sphincter fail to unite properly, either a second operation must be performed, or the patient will suffer from some degree of anal incontinence—a constant source of potential embarrassment. When fistulae are extensive, the scar tissue laid down after this type of operation may be such that the patient is seriously handicapped either in sphincteric control or else by virtue of stenosis. Therefore, it seemed very desirable to develop a surgical technic in which it would be possible to excise the tract and close the wound so that healing by primary intention would take place, and, thus, avoid the many undesirable features associated with the methods now employed. This has been done. Twelve patients have had a fistula in ano resected and the operative wound closed tightly, with healing by primary intention in 11 cases. In the twelfth case, the procedure to be described was not followed in all of its component parts. The convalescent period in the 11 cases was marked by its freedom from pain or discomfort, its shortness, the absence of drainage, and the lack of need for time-consuming care and treatment. There have been no recurrences during follow-up periods of from two to six months.

## MATERIAL

The patients were all young adults between the ages of 18 and 31. Each had a history of an acute ischiorectal abscess which had had to be incised and drained. This had been followed by either one or more recurrences of the abscess or else by fairly persistent drainage from the site of the original incision. When first examined, each patient presented a true fistula in ano, with an

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external orifice from which pus could be expressed and through which a probe could be passed and manipulated into the anal canal. Several patients had one or more branches to the primary tract.

## METHOD

The patients are prepared for the operation in the usual manner, by sitz baths, low-residue diet, sulfasuxadine, and castor oil the afternoon preceding surgery. The evening preceding surgery the tract is injected with methylene blue in an effort to stain it so that all branches of the main fistulous tract can be readily identified during the operation. If it is believed that multiple tracts are present, the external orifice is injected with lipiodol and roentgenograms taken. All operations are performed in the flexed, prone position, under either spinal or caudal anesthesia. After suitable preparation and draping of the operative field, a malleable, blunt-tip probe is passed along the tract and gently manipulated until it enters the anal canal through the internal orifice of the tract. The probe is then bent so that it forms a circle, and, thus, cannot be dislodged during the operation. A small elliptical incision is made around the external orifice down to subcutaneous tissue and one limb carried toward, but never across, the mucocutaneous juncture. A second small elliptical incision is made through the mucosa around the internal orifice, but skin and mucosal incisions are not joined. With a small, sharp, curved, dissecting scissors and a small knife (No. 15 Bard-Parker), the tract is gently dissected free from the surrounding structures, using the probe as a guide. Gentle traction assists in this. The tract is followed over, through, or under the external anal sphincter, doing as little damage as possible to this muscle. When the muscle is cleared from the tract, the internal orifice is attacked and dissection begun there and carried down until the tract is entirely freed, and can be removed *in toto*. The wound is carefully inspected for residual scar tissue, or for an undiagnosed limb of the fistula, either of which must be excised if present. Complete hemostasis is secured using Nos. 80 or 120 cotton ties. The tissues of the wound are then infiltrated with a penicillin solution, 2000 units per cc., using 20 to 100 cc. to insure equal and thorough diffusion throughout all the tissues. The dead space is very carefully obliterated with interrupted sutures of Nos. 60 or 80 cotton, repairing at this time any damage done to the sphincter. As it is of utmost importance that every vestige of dead space be obliterated, these should be fairly close together; as a rule, two or three layers will be necessary. The cut-edges of mucosa are carefully approximated with several Nos. 4-0 chromic catgut sutures on an atraumatic needle, and the skin edges are approximated with No. 60 cotton, using vertical mattress sutures in each instance. No drains are used. The postoperative regimen consists of a low-residue diet for 3-4 days, mineral oil daily, morphine, ice bag to the perineum for pain, and if no bowel movement occurs by the fourth day, an oil retention enema is given, followed by milk of magnesia orally. The patients are allowed to get out of bed on the second postoperative day, and discharged from the hospital shortly afterwards. The skin sutures are removed between the 5th and 7th postoperative days.

The essential points of the procedure, thus, are: (1) accurate localization of the tract; (2) careful, neat dissection; (3) infiltration of the wound with penicillin; (4) complete hemostasis; (5) careful obliteration of the dead space with fine cotton sutures; and (6) complete closure of the mucosal incision. It is believed that if the technic outlined above is exactly followed, the results obtained can be readily duplicated.

<div align="center">RESULTS</div>

Of the 12 patients operated upon by this method, 11 have healed by primary intention. There has been very little edema of the wound; only mild postoperative pain; and there has been no drainage. There were no instances of even temporary anal incontinence. Nine patients were followed six months, or longer, and three patients were followed for two months. None have showed any evidence of recurrence of the fistula in ano. The one patient who did not heal *per primam* was not injected with penicillin at the time of operation. He complained of more discomfort than the average patient, and about the 5th postoperative day, the wound was red and swollen. Removal of the skin sutures permitted pus to escape. Drainage persisted until one or two cotton sutures were removed from somewhere in the depths of the wound, following which the wound healed. Letter follow-up indicates he has no apparent evidence of a fistula, but this case is classified as unsatisfactory. It illustrates perfectly the point that the outlined technic must be followed exactly if complications are to be avoided.

DISCUSSION.—It is accepted by all surgeons that primary union is the ideal to strive for in any wound, traumatic or operative. This, because, when healing is by second intention, one must frequently contend with such undesirable features as infection, excessive scar formation, with consequent tissue distortion and malfunction, painful dressings, prolonged convalescence, and after fistulectomy, possible temporary or permanent anal incontinence. Furthermore, the scarring, distortion, malfunction, or in cases of fistulectomy, the anal incontinence, may require correction by secondary plastic procedures. It is recognized, of course, that certain wounds, for reasons inherent in themselves such as the repeated and heavy contamination that occurs around the rectum do not readily lend themselves to primary closure. Nevertheless, one should continually try to find new methods, or to apply recent advances, to the treatment of such wounds, in order that more of them, without increasing the risk to the patient, may be closed with a reasonable expectation of securing primary union. The method described in this paper does make possible the obtaining of primary union after resection of a fistula in ano. In addition to the common surgical principles of neat, clean, nontraumatic dissection and careful obliteration of all dead space, penicillin is carefully infiltrated into all of the tissues comprising the wound. The underlying principle of this procedure is to inactivate the bacteria in these areas, which, while not sensitive to the ordinary tissue concentration of penicillin secured by parenteral injection, presumably are inactivated by the extremely high concentration obtained in this manner.[1]

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Cotton is used in preference to catgut because of the minimal tissue reaction to this material and, hence, less necrotic material to serve as culture media for the various organisms.

Admittedly, the group treated is not large enough to permit any final evaluation of the method. However, it is a fact that 11 of 12 cases did heal by primary intention, and that the one failure was in the patient whose tissues were not injected with penicillin. This, in itself, indicates that the method should be practical if followed exactly. Furthermore, there have been no recurrences over follow-up periods of two to six months, probably a sufficient period of time for such cases. This would seem to indicate that the method is curative. There is no logical reason why there should not be just as many cures when fistulae are treated in this way, as by the method of laying them open to granulate in, provided all of the tract is excised.

There is also a great saving to the patient economically, because of early release from the hospital, lack of need to return for daily dressings, and the fact that he can return to his normal activities without experiencing the discomfort present when there is a raw, granulating, anal wound.

### SUMMARY AND CONCLUSIONS

A successful method has been described by which it is possible to secure primary wound healing after the resection of a fistula in ano. The essential points in the procedure are: (1) accurate localization of the tract; (2) careful, neat dissections; (3) infiltration of the wound with penicillin; (4) complete hemostasis; (5) careful obliteration of the dead space with fine cotton sutures; and (6) complete closure of the mucosal defect. Eleven of 12 cases so treated have had primary union of their wounds, and there have been no recurrences of the fistula in the 12 patients over periods of two to six months. The convalescent period was marked by its shortness, and absence of complications. The method described is preferable to those commonly employed in which healing is by second intention because it eliminates: (1) excessive scarring; (2) anal incontinence; and (3) prolonged convalescence.

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# THE EFFECT OF HEPARIN UPON INTRA-ABDOMINAL ADHESIONS IN RABBITS

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IT IS GENERALLY RECOGNIZED that certain patients form intra-abdominal adhesions after operation or after inflammatory processes. These may produce intestinal obstruction, and at times require surgery. Often adhesions reform and, again, cause obstruction. Methods that might prevent formation or reformation of adhesions have been the subject of several investigations adequately reviewed by Boys[1] in 1942.

Certain of these methods have been of general interest. Rea and Wangensteen,[2] Gepfert,[3] Totten,[4] Merkle,[5] and others, introduced amniotic fluid, saline, air, oil, glucose, blood, gum acacia, *etc.,* into the peritoneal cavity to mechanically separate damaged surfaces until reëpithelization might occur. Ochsner and Garside,[6] Donaldson,[7] Ward,[8] and others, tried proteolytic enzymes, such as papain or trypsin to digest deposits of fibrin. Lehman and Boys[9, 10] employed heparin to minimize the formation of fibrin. Clinical reports of the use of papain by Ochsner,[11] and of heparin by Lehman and Boys[12, 13] and Massie,[14] have offered encouragement, but the results are not easily evaluated.

Experiments have, therefore, been undertaken to further study the effect of heparin upon the formation and reformation of adhesions. Rabbits, usually male, have been used for all experiments.

## EXPERIMENTAL METHODS

*Operations for Production of Adhesions:* Rabbits were anesthetized by intravenous sodium amytal. A midline incision was made, using sterile technic. The appendix was exposed and freed from the meso-appendix using fine silk No. 000000, for ligation of vessels. The antimesenteric surface was then seared by applying a thin, heated spatula. The peritoneum and the incision were closed by a continuous mattress suture of either fine silk or catgut. The skin was closed with interrupted silk. Operations were performed by several individuals employing this standard technic.

*Operations for Division of Adhesions:* Celiotomies were performed through the same midline incision two weeks, or more, after the searing and at varying intervals thereafter, to determine occurrence and extent of adhesions and to divide and study reformation of adhesions. Adhesions were divided, using blunt dissection for closely adherent surfaces or sharp dissection with division and ligation for longer bands.

The extent of adhesions was determined by estimating the length of bowel involved and at times also by comparison of serial photographs. The length of extensively-involved matted segments of bowel was empirically estimated as 20 cm. The abdomen and chest were examined by autopsy in all animals that died. Histologic examination was made on the appendices of all animals sacrificed or dying within ten days of the original searing, and on other viscera that exhibited gross pathologic change.

*Technic of Control Experiments:* Adhesions were examined at operation in two control series, but not divided. These adhesions were later observed at operation or autopsy. In a second control series the adhesions were divided without using any form of therapy and later reëxamined.

*Method of Study of Heparin and the Formation of Adhesions:* The effect of heparin on formation of adhesions was studied by searing the appendix and immediately placing 15 mg. of heparin into the abdomen. A second intraperitoneal injection of 15 mg. of heparin was given 24 hours after operation. In each instance the heparin was diluted by 30 cc. of normal saline. Heparin in Pitkin's menstruum* (100 to 200 mg.) was placed in the abdomen at the time of searing in another group of rabbits.

*Method of Study of Reformation of Adhesions.—Control Experiments:* Reformation of adhesions was investigated in control experiments by administering 30 cc. of normal saline intraperitoneally at the time of division and then twice a day by needle puncture for 72 hours. Gelatin, 5 per cent in sterile $H_2O$, was similarly injected in another control series. The state of the adhesions was determined by subsequent operation or autopsy 7 days to 4 weeks, average 2 weeks, after division.

*Methods of Study of Reformation of Adhesions.—Test Experiments:*

(A) *Heparin in Saline:* Heparin was administered in a volume of 20 to 30 cc. of saline at the time of division of adhesions and subsequently at intervals during 72 hours by reinjection through the abdominal wall. Peripheral clotting time was determined on venous blood at intervals of two to four hours by the capillary-tube method. The initial 20 to 30 cc. of saline contained 5 to 60 mg. of heparin, usually 15 mg. Subsequent injections contained similar amounts of heparin. The usual total dose was around 200 mg. Intervals between injections were varied to maintain a prolongation of the clotting time always over two minutes and usually over 15. Maximum prolongation of clotting time was often one-half to two hours. Reformation of adhesions was studied during operation or autopsy in animals surviving seven to 60 days.

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* The ingredients of the Pitkin menstruum are gelatin 15 to 30 per cent, dextrose 5 to 12 per cent, glacial acetic acid 0.5 per cent and sufficient distilled water to make 100 per cent. The formulae used in our paper were LP-8, LP-9, and LP-10. A reference for this information is: Loewe, *et al.:* Venous Thrombo-embolic Disease, J. A. M. A., Vol. 130, 388, February 16, 1946.

Heparin and saline (10 to 50 mg.) was also administered at the time of searing and again by intra-abdominal injection at 24 hours in a group of rabbits.

(B) *Heparin in Pitkin's Menstruum:* Twenty-five to 200 mg. was placed in the abdomen at the time of operation and subsequently injected during 72 hours at intervals determined by the peripheral clotting time. The usual total dose was around 300 mg. Prolongation of clotting time was maintained at levels similar to those described with heparin and saline. Heparin in Pitkin's menstruum (150 mg.) was used as a single dose at the time of searing and also at the time of division of adhesions in other rabbits.

### EXPERIMENTAL RESULTS
#### FORMATION OF ADHESIONS

*Production of Adhesions:* One hundred and fifteen rabbits survived operation and searing of the antimesenteric surface of the appendix without infection. Of these, adhesions developed in 89. Twenty-six rabbits did not develop adhesions. Eighteen of the 26 were again treated by searing. Five developed minimal adhesions. Three developed adhesions only after the third searing.

*Formation of Adhesions:* Adhesions developed in 15 of 21 rabbits in which heparin had been placed in the abdomen at the time of searing of the appendix and again injected 24 hours later. The appendices of five of the six animals that did not develop adhesions were again seared and when reëxamined there were no adhesions. Adhesions developed in three of five rabbits in which heparin in Pitkin's menstruum had been placed in the abdomen at the time of searing. In five additional instances single doses of heparin in Pitkin's menstruum were administered at the time of searing. Adhesions formed in three.

*Duration of Adhesions:* Seven rabbits were explored two weeks after searing, without dividing adhesions. Celiotomy 33 to 51 days later revealed no evidence of change in the amount or character of adhesions.

*Control Experiments—Reformation of Adhesions:*

Reformation of adhesions was studied in the 89 rabbits that developed adhesions after the first searing. Since these rabbits were subjected to a series of operations during which adhesions were examined or divided and treated, or not treated, by control or test substances, and since they often served for from two to seven consecutive experiments the results will be reported as groups of experiments and not as individual animals. Animals dying within a week of operation, or developing infection, are not included in the experimental results.

(A) *Division of Adhesions without Treatment:* Adhesions were divided in 18 experiments and subsequently reëxamined. They reformed in all but one rabbit. The length of large and small intestine involved in adhesions before division varied from the attachment of a single band up to 20 cm.,

average 6.9. After division the length varied from one band to 20 cm., average 9.0 cm. The extent of the adhesions observed after redivision had increased over that before division in ten experiments and decreased in eight.

(B) *Normal Saline:* Adhesions were divided and treated initially by 30 cc. of saline and subsequently by intraperitoneal injections of saline during 72 hours in five experiments. In four, adhesions reformed. The extent of adhesion before division varied from 2 to 20 cm., average 8. After division and treatment by saline the length of involvement varied from 0 to 10 cm., average 5. The extent of adhesions after treatment increased in two experiments and decreased in three. The rabbit that did not have adhesions after saline treatment had 20 cm. before division.

(C) *Gelatin:* Gelatin was used after division of adhesions in six instances and in five adhesions redeveloped. Before division of adhesions the length of involvement was from 2 to 18 cm., average 7. After treatment the length varied from 0 to 10 cm., and averaged 6. The extent of involvement increased in three and decreased in three. The animal that did not redevelop adhesions had one 3 cm. band at the time of division.

### Experiments with Heparin—Reformation of Adhesions:

(A) *Heparin in Saline:* In 20 experiments adhesions were divided and treated during 72 hours by heparin in saline. Adhesions reformed in 17. Before division and treatment adhesions involved 1 to 20 cm. of bowel, average 8. Afterward they involved 0 to 20 cm., average 6. The amount of involvement increased in ten, decreased in eight, and was unchanged in two. The three animals that had no adhesions had had 1, 4, and 10 cm., respectively, at the time of division.

In addition to the 20 successful experiments there were eight deaths. Three were caused by hemorrhage.

(B) *Heparin in Pitkin's Menstruum:* In 21 instances heparin in Pitkin's menstruum was employed during the first 72 hours after division of adhesions. They redeveloped in 19. The area of involvement before division and treatment varied from 2 to 20 cm., average 8.3 and afterward from 0 to 20, average 6.6 cm. The extent of adhesions increased in six, decreased in 11, and was unchanged in four. The two animals that did not redevelop adhesions had 4 and 10 cm., respectively, at the time of division of adhesions.

In four instances with single doses of heparin in Pitkin's menstruum given at the time of division of adhesions, all reformed them. The area of involvement varied from 6 to 15 cm., average 9, before treatment and afterward 2 to 20 cm., average 13. The extent increased in three and decreased in one.

In addition to the 25 successful experiments reported above there were 22 deaths during administration of heparin in Pitkin's menstruum. Of these 17 died of hemorrhage.

*Pathologic Examination.*—Autopsies were performed on 15 rabbits sacrificed at intervals within ten days of searing of the appendix. Autopsies were also performed on 30 animals dying during or just after a 72-hour period of

treatment with heparin. Treatment was begun immediately after division of adhesions.

Gross examination of the 15 sacrificed rabbits often revealed fibrinous adhesions about the appendix. Material for staining and preparation for microscopic study was obtained from cross-sections of the appendix. Microscopic preparations satisfactory for study of mesothelium were obtained in
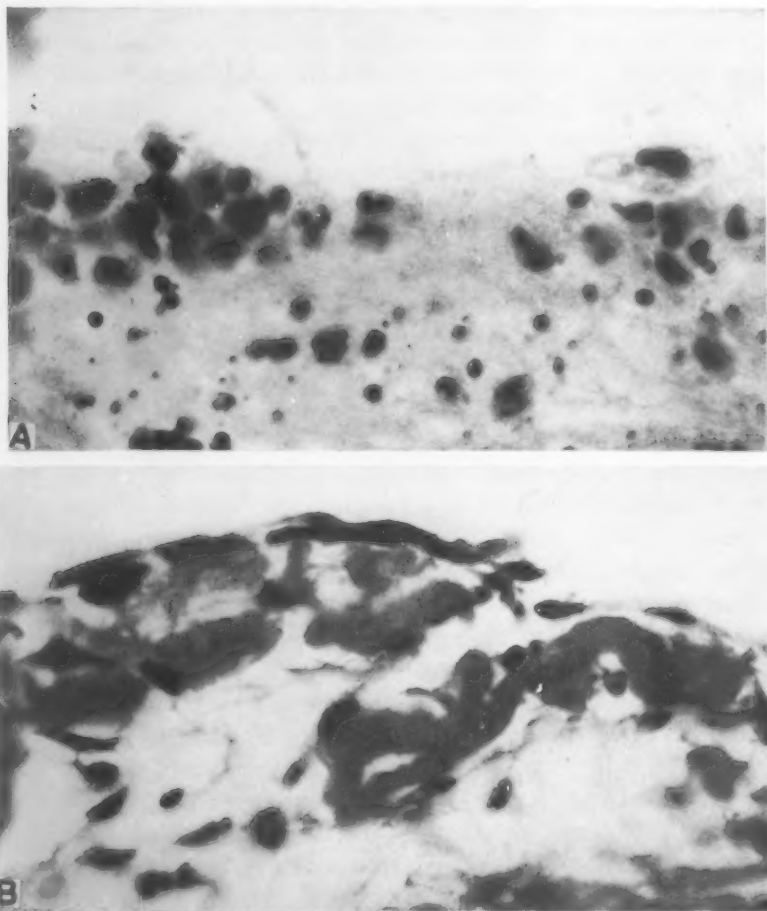


FIG. 1.—(A) Fibrinous surface of appendix 18 hours after searing. (B) Fibrin covered by a single layer of flat cells resembling mesothelium 96 hours after searing.

only seven. Of these, two, six and 22 hours after searing, had no visible mesothelium. The burned surface was covered by fibrin (Fig. 1 A). Two, at 18 and 42 hours, had a few isolated cells resembling mesothelial cells on the surface of the fibrin over the burned area. Three, at 30, 72, and 96 hours had continuous sheets of single-layered cells, resembling mesothelial cells, over the granulating surface (Fig. 1 B).

Gross examination of 30 rabbits that died during the period of heparin therapy revealed massive hemorrhage into the abdomen or into the wound in 20. Satisfactory microscopic examinations of the appendices at the area of division of adhesions were possible in five of nine rabbits studied. Fibrinous exudate or fibrin was present in each. Sections of lungs of 12 showed advanced pulmonary edema. Congestion was also present in five, and hemorrhage in three. Brain tissue was examined in three and there were small hemorrhages in the pia mater of the cortex of two. One of two hearts examined showed small subendocardial hemorrhages in the left ventricle.

TABLE I

SUMMARY OF STUDIES ON ADHESIONS

| | No. of Experiments | No. that Developed Adhesions | % that Developed Adhesions | Change of Extent of Adhesions (Average) | | Number of Animals Exhibiting Change | | |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| | | | | Before | After | Increase | Decrease | No Change |
| Formation of Adhesions: | | | | | | | | |
| No treatment......... | 115 | 89 | 77% | ..... | ..... | .. | .. | .. |
| Heparin in saline...... (2 doses) | 21 | 15 | 71% | ..... | ..... | .. | .. | .. |
| Heparin in Pitkin's menstruum (1 dose).. | 5 | 3 | ....* | ..... | ..... | .. | .. | .. |
| Reformation of Adhesions: | | | | | | | | |
| No treatment......... | 18 | 17 | 94% | 7 cm. | 9 cm. | 10 | 8 | 0 |
| Heparin in saline...... (72 hours) | 20 | 17 | 85% | 8 cm. | 6 cm. | 10 | 8 | 2 |
| Heparin in Pitkin's menstruum (72 hours) | 21 | 19 | 90% | 8 cm. | 6 cm. | 6 | 11 | 4 |
| Heparin in Pitkin's menstruum (1 dose).. | 4 | 4 | ....* | 9 cm. | 13 cm. | 3 | 1 | 0 |
| Saline alone.......... | 5 | 4 | ....* | 8 cm. | 5 cm. | 2 | 3 | 0 |
| Gelatin 5% aqueous solution........... | 6 | 5 | ....* | 7 cm. | 6 cm. | 3 | 3 | 0 |

* Series not large enough to warrant percentage.

DISCUSSION.—The summary in Table I demonstrates that the likelihood of developing adhesions was almost as great in the rabbits treated by heparin as in those that were not treated, or were treated by saline or gelatin. There was no significant difference in the average extent of involvement of bowel by adhesions or in the numbers of rabbits that had an increase or a decrease in the amount of adhesions.

It has been suggested by Lehman and Boys,[9, 10] and others, that heparin might prevent or minimize the formation of fibrin and the development of adhesions. Our histologic studies in rabbits dying of hemorrhage during heparinization revealed fibrinous exudate or fibrin at the site of injury.

Although Brunn,[15] Clarke,[16] and Hertzler[17] have studied regeneration of mesothelium, there is no definite evidence determining the rate of growth. Mesothelium has been described as originating from the edges of defects or as developing by a differentiation of connective tissue cells (Baily[18]). Since

young mesothelial cells are easily lost in preparation of tissue for microscopic study and since it is difficult to differentiate mesothelial cells from flattened wandering cells in cross-section preparations, our histologic studies have not solved these problems with certainty. It seemed, however, that reperitonealization may require a period of time longer than the maximum of 72 hours used for treatment in these and other experiments.

## CONCLUSIONS

1. Heparin in large doses, continued up to 72 hours, has not prevented the formation or reformation of intraperitoneal adhesions or the deposition of fibrin on the surface of injured appendices in rabbits.

2. There was a spontaneous failure of development of adhesions in 23 per cent of the rabbits used in this experiment. There were also 6 per cent of the rabbits subjected to division of adhesions, and no other treatment, that did not redevelop adhesions. Heparin increased the likelihood of not developing adhesions by less than 8 per cent.

3. The extent of the adhesions that redeveloped after division and heparinization was equal to that observed in control experiments.

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# THE QUESTION OF REGENERATION OF NERVE FIBERS TO THE HUMAN ADRENAL GLAND AFTER BILATERAL SYMPATHECTOMY*

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THE INEFFICACY of the medical treatment of hypertension was the prelude to the search for other, more potent means, of dealing with this widespread and inevitably fatal disease. In 1924, N. Pende presented before the Congress of Internal Medicine, at Padua, his conception of a surgical procedure based upon the observation that resection of the left splanchnic nerve resulted in an atrophy of the adrenal gland and a diminution of the secretion of epinephrine. From then on, this addition to the therapeutic arsenal was developed and perfected by Leriche and Wertheimer, in France, and Peet, Smithwick, and others, in this country. Its physiologic basis is yet to be established, and the procedure itself has frequently been criticized because of the reported regeneration after experimental sympathectomy in animals. In man, Rogoff[1] has reported a case of Addison's disease following sympathectomy.

The statement has been made several times[2, 3] that the present-day sympathectomy for hypertension completely denervates the adrenal glands. Insofar as I know, this has never been proven in the human. Smithwick[4] has ascribed the rise in blood pressure in the weeks following sympathectomy to the "regeneration of the interrupted vasoconstrictor pathways." To my knowledge, its actual demonstration in man has never been undertaken. If regeneration of these resected nerve fibers occurs, one might demonstrate this in an end-organ, such as the adrenal gland. The anatomic method was selected as a means of approach, and, therefore, a study was undertaken to determine the extent, if any, of regeneration of sympathetic nerve fibers to the human adrenal gland following bilateral sympathectomy.

The innervation of the human adrenal gland is still not completely understood, perhaps largely for technical reasons. In 1944, I made a comprehensive study of the innervation of the normal adrenal gland of man, and other forms. The adrenals of man receive their innervation through the greater and lesser splanchnics and from the neighboring ganglia. This innervation is mostly preganglionic, with some postganglionic fibers coming from the solar plexus. The presence of numerous ganglion cells in the human medulla would indicate the presence of an additional postganglionic innervation.[5] From this brief review, one may draw a working hypothesis that bilateral splanchnicectomy and thoracolumbar sympathectomy should produce a complete degeneration of the preganglionic fibers of the gland, with only the postganglionic fibers remaining. The effect on the ganglion cells would remain to be determined.

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* Read before the New York Pathologic Society, April 25, 1946.

The anatomic and physiologic experimental evidence has, for the most part, been contradictory, partly the result of failure to interpret differences in species and partly due to variations in experimental technic. Elliott,[11] Hollinshead,[12] Swinyard,[13] and Young,[14] in the cat, have shown that the innervation of the chromaffin tissue is preganglionic with few or no postganglionic fibers. In my own experiments on the rabbit, the fibers of the adrenal were almost completely degenerated seven days after infradiaphragmatic splanchnic resection. However, I also found some crossed innervation; this may be peculiar to rabbits. From an anatomic standpoint, Hollinshead and Finkelstein[15] showed that regeneration to the ipsilateral gland occurred in cats following unilateral sympathectomy and splanchnicectomy as early as the 2nd month, and at the 5th month an apparently normal innervation existed.

Bacq and Dworkin[16] in two of three cats, one year after total bilateral sympathectomy, found physiologic as well as anatomic evidence of regrowth of preganglionic fibers. Hodes,[17] working in Cannon's laboratory, found that 30 days after sympathectomy physiologic evidence seemed to point to a regrowth of fibers to the adrenal medulla. This author wisely pointed out the possibility of the intervention of other fibers in his experimental results. Haimovici and Hodes[18] performed a total sympathectomy upon seven cats. Their physiologic criteria indicated sympathetic regrowth in all animals. They emphasized that in order to keep regeneration at a minimum the greatest possible preganglionic destruction should be carried out. Maes and Simeone,[19] working with cats, crushed the splanchnics in the chest and beneath the diaphragm. From the degree of physiologic response they concluded that regrowth of fibers must be considered six weeks after operation. In all of these physiologic studies, anatomic data were lacking, or inconclusive.

Numerous experiments on dogs by Hermann, and his school,[20, 21, 22] in France, have suggested that the endocrine elements show no morphologic changes following complete sympathectomy, and that minimal amounts of epinephrine were still present.

Of the more recent papers, that of Papez, Jensen, and Dukes[23] is enlightening. Two years after complete sympathectomy in dogs, they found only a minimal amount of regeneration, not in excess of 5 per cent. There were some postganglionic fibers coming from the neighboring ganglia which were not affected by the operation. In addition, they found a few end-bulbs, and thickened endings in the medulla.

### CLINICAL SUMMARIES

Case 1.—E. B., a 45-year-old white male gave a three-year history of dyspnea on exertion, dizziness, headaches, and failing vision, all becoming more marked in the few weeks before admission. Physical examination showed a blood pressure of 260/155, with an enlarged heart and slightly enlarged liver. The eye grounds were typical of severe hypertensive retinopathy. The urine contained two plus albumin, with a few red cells and rare white blood cells. Kidney function tests were within normal limits. The electrocardiogram was suggestive of myocardial damage.

Right sympathectomy on 11/19/'43: The greater and lesser splanchnics from T 8 down to, and including, the semilunar ganglion, as well as the sympathetic trunk from

T 8 to L 2 were removed. Many of the branches of sympathetic chain were excised as well. Left sympathectomy was done on 12/3/'43; the operation was the same as on the right side.

Pathologic Report: Fragments of nerve and ganglia without significant change.

The postoperative blood pressure was 180/120, with pronounced orthostatic hypotension. Postoperative recovery was uneventful. On June 15, 1945, the patient was admitted to the New York City Hospital for recurrence of symptoms of a four-month duration. The blood pressure was 235/140 and rose at one time during his stay to 255/140. His course was downhill, and he died August 13, 1945 in uremic coma (NPN-210), 19.5 months after operation. The postmortem done five and one-half hours after death, showed pulmonary edema, cardiac hypertrophy, bilateral chronic adhesive pleuritis, and arteriolar nephrosclerosis.

**Case 2.**—S. R. This was a 50-year-old white male, with a three-year history of convulsive seizures, syncope, and severe headaches. The blood pressure varied from 180/100 to 210/110. The heart was enlarged, and the electrocardiogram showed moderate myocardial damage. The urine contained one plus albumin, and showed some white blood cells. The kidney function tests were normal. Spinal tap was negative. The diagnosis of hypertensive encephalopathy with essential hypertension was made and sympathectomy was advised.

Right sympathectomy on 5/31/'45: The sympathetic trunk from T 9 to L 2, as well as all communicating branches were resected. The greater and lesser splanchnics were isolated from T 6 down to, but not including, the semilunar ganglion, cut, and excised. Left sympathectomy was done on 6/18/'45; the same procedure was repeated.

Pathologic Report: The nerves and ganglia showed some changes, which, however, are within normal limits.

Postoperatively, the blood pressure dropped to 170/100, and recovery was without incident. However, the symptoms remained, and the blood pressure rose rapidly to the preoperative levels. The patient died on January 15, 1946, seven months after operation. The autopsy done 36 hours after death, showed subdural hemorrhage, cardiac hypertrophy, moderate coronary sclerosis, and arterial as well as arteriolar nephrosclerosis.

Clinically, sympathectomy was undertaken in each case with the hope of arresting the advance of the disease. In both cases, the blood pressure reached the preoperative level before death. It is of interest to note that the pathologic report of the resected nerves and ganglia was essentially negative. Studies, which Dr. J. A. Lisa and I have undertaken of this material, using various staining methods, seem to indicate that there is some deviation from the normal in the splanchnic nerves and sympathetic ganglia removed from hypertensive patients at operation. Whether this is a primary phenomenon or secondary to the generalized arteriolar disease, from which many of these patients suffer, remains to be determined.

### MATERIALS AND METHODS

Slices of an average width of two to three millimeters were taken from each gland and impregnated with silver, according to the method of A. Weber.[8, 9] Serial sections were made of the totality of each slice, at ten micra per section; all sections were examined. This method permits tracing the exact distribution of nerve fibers as they enter the adrenal gland, as well as an accurate study of the ganglion cells. It is probable that frequent errors in the quantitative study of ganglion cells in the human adrenal are due to methods where serial sections are made and only one in every five or ten are

examined. Thus, one can see why ganglion cells, having a thickness of only 10 to 20 micra can easily be missed, or thought to exist in small numbers only. Many fields were examined under high power and oil immersion. Adrenals coming from patients who had not undergone sympathectomy served as controls, and these slices were processed in the same batches as the other material.

### OBSERVATIONS

Before describing my own results, it is necessary to say that the use of silver stains allows one to distinguish between pre- and postganglionic fibers. This has been demonstrated anatomically by Weber,[8] and Nonidez and Hare.[24] In the sections the preganglionic fibers are dark brown, and the postganglionic fibers are light brown.

The first very striking observation in the two cases of this study was the almost complete absence of nerves in the medulla. The usual picture of interlacing and branching fibers, or fine fibrils, found in the sections of normal adrenal medulla was not seen. Occasionally, a few very fine fibrils were encountered, and, here and there, a nerve trunk. Otherwise, search of field after field revealed no nerves (Figs. 1 and 2). The fibers that were present were almost entirely light brown, therefore, postganglionic, and only rarely was a preganglionic fibril noted. At places where the nerve trunks were traced into the cortex and medulla, wide spaces were apparent between the pale brown fibrils, corresponding, without doubt, to the absent preganglionic fibrils (Figs. 3 and 4). In most instances the remaining nerves entered the gland together with blood vessels. They pass through the cortex and eventually break up to distribute themselves in the medulla. There, fine postganglionic nerve endings were encountered on the walls of the vessels.

Ganglion cells can be found in the normal adrenal of man in three places: in the ganglia of the capsule, in nerves as they pass through the cortex and medulla, and in the medulla.[5] They are usually in groups, but may be found isolated or in the path of a fiber. Their intensely-stained cytoplasm, with a large pale nucleus and numerous dendritic processes make them easily identifiable (Fig. 1). The dense intercellular plexus formed by the branching of the arriving preganglionic fibers is very striking. They form synaptic endings on the ganglion cell itself.

After sympathectomy the picture is quite different. In both cases the numerous dark interlacing preganglionic fibers are absent, and the ganglion cells look peculiarly isolated, nevertheless, retaining their normal characteristics (Fig. 2). Their argyrophilia, however, seems to be slightly diminished. Other findings of a more morphologic nature, such as swellings of nerve endings; or nerve fibers; and rarity of giant nerve endings have been briefly reported elsewhere.[6]

DISCUSSION.—It is obvious that in these two cases there has been virtually no regeneration of the nerve fibers in the adrenal gland. What is the nature of the remaining fibers in the medulla? The postganglionic fibers in any case would not have been directly affected by the operation. However, the presence
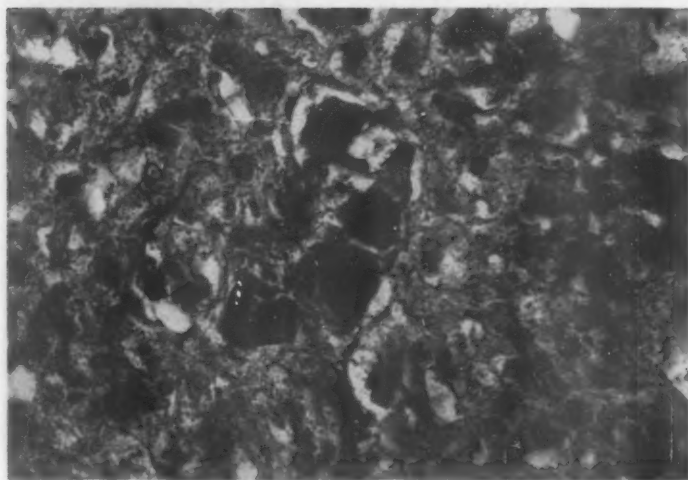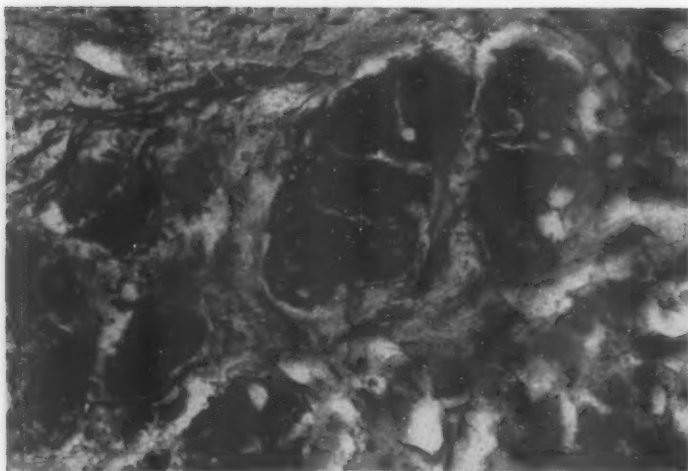
FIG. 1



FIG. 2

FIG. 1.—Normal adrenal gland (control).
Ganglion cells with dark brown preganglionic fibers. A nerve trunk is in the upper left, and the medulla at the lower right; fine nerve fibrils are visible in the latter. The somewhat separate-appearing round area at the right upper margin of the uppermost of the group of four ganglion cells is a giant nerve ending. ($\times$ 95)
All sections are 10-micra thick, and stained according to the Weber silver technic.

FIG. 2.—Adrenal after bilateral sympathectomy.
Group of pale ganglion cells in the medulla. The interlacing plexus of preganglionic fibers has all but disappeared, and the surrounding medulla is devoid of fibers. ($\times$ 160)

of the very few dark brown preganglionic fibers raises the question as to whether they are regenerated fibers or are fibers which have escaped degeneration. In their experiments on dogs, Papez, and his co-workers, felt that the
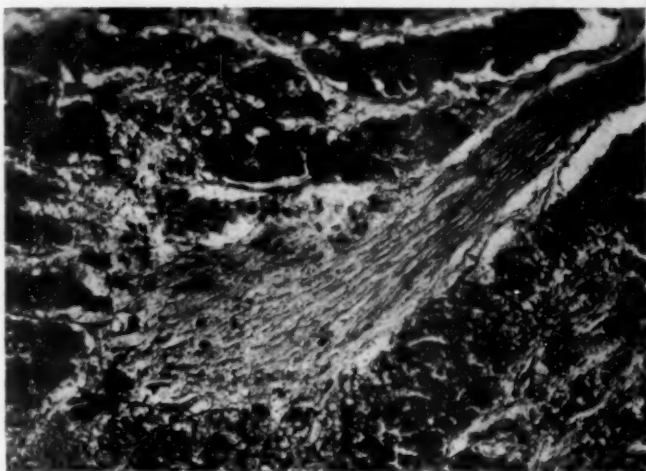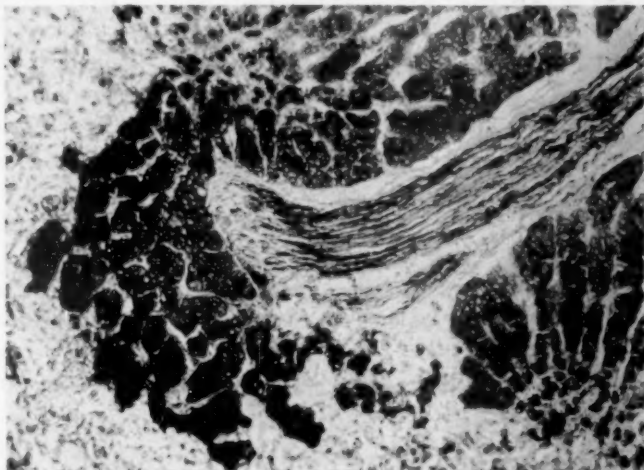
FIG. 3



FIG. 4

FIG. 3.—Normal adrenal gland (control).
Nerve trunk composed of preganglionic fibers passing through the cortex towards the medulla. ($\times$ 360)

FIG. 4.—Adrenal after bilateral sympathectomy.
The preganglionic fibers have disappeared and one sees only the more pale-staining postganglionic fibers. ($\times$ 360)

number of normal fibers seen in the adrenal medulla two years after operation did not exceed those of the recently subtotally sympathectomized dog. They stated, however, that these were probably postganglionic fibers. My own obser-

vations based on staining differences between pre- and postganglionic fibers indicate that some of the remaining fibers are certainly preganglionic. It would seem that these are fibers which have escaped degeneration.

From a theoretic standpoint, the extent of the resection in these two cases makes regeneration over such a wide distance a very questionable occurrence. As Weber[10] has shown, even when the two cut-ends of a nerve fiber lie within a short distance of each other, their reunion is a matter of chance. In addition, he states: "The greater the distance between the cut-stumps of the nerves, the greater the phenomena of negative neurotropism." Experimental evidence by Papez, and his group, indicates that after two years "the regeneration of splanchnic and sympathetic nerves after total sympathectomy is relatively small, and far smaller within the gland than suggested by the size of the regenerated false nerve trunks when no histologic examination is made." They also stated that "the process of regeneration of nerve fibers to the gland seemed to be fortuitous, variable, and at best very scanty." The study of my two human cases is in accord with their microscopic observations on dog adrenals.

Rogoff's contention, in his widely cited paper,[1] that "denervation of the gland by section of its nerves is usually followed by regeneration of the nerve supply within a few weeks" is contradicted by the observations of this study. It would be more logical to assume that the Addison's disease in his report was the result of interruption of the vascular supply to the gland. Besides, only the deepest layers of the reticular zone are innervated.[5]

The absence of degeneration of the ganglion cells lends support to the synaptic theory of nerve conduction. The normal histologic picture of the secretory elements of the adrenals of both cases confirms the findings of previous investigators.[21, 22, 23] Unpublished observations indicate that this is not altogether the case in the first days after sympathectomy.[7] The rarity of giant nerve endings, which are a constant occurrence in the normal adrenal medulla of man, leads one to suspect that they are endings of preganglionic nerve fibers.

### CONCLUSIONS

(1) In two cases of human hypertension, following extensive bilateral sympathectomy, there were only a few nerve fibers left in the adrenal glands. These were mostly postganglionic fibers.

(2) The postoperative return to hypertensive levels of the blood pressure following sympathectomy cannot be explained by regeneration of nerve fibers into the adrenal gland.

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# RETROPERITONEAL CYSTS

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Retroperitoneal cysts have been defined by Handfield Jones[10] as those cysts lying in the retroperitoneal fatty tissues which have no connection with any adult anatomic structure save by areolar tissue. The rarity of retroperitoneal cysts, the speculation as to their exact origin and the uncertainty of their diagnosis makes them among the most interesting of all abdominal tumors. While a good many isolated case reports of these cysts of one type or another appear in the literature, there is an apparent lack of unanimity among various authors as to the origin of these cysts. The case report herewith appended is a rather typical-one, in which the diagnosis was made preoperatively.

**Case Report.**—Miss M. B., a white female, age 26, was first seen on January 21, 1944, at which time she complained of soreness and a lump in the right lower abdomen. The patient does not remember having symptoms until about November, 1943, when she first had soreness occasionally across her lower abdomen. She thinks she has had vague pains for three or four years, but she did not feel the lump there until this time. There has been no weight loss and no change in bowel habits, no change in periods. Wearing tight garments across the waist causes some discomfort. There is no change in the tumor with the menstrual cycle or with gastro-intestinal or urinary functions. She thinks the tumor has very gradually grown a little larger. The past history and review by systems was not pertinent.

Physical examination revealed a tall, thin girl, appearing quite healthy, with normal pulse, temperature, and a blood pressure of 100/80. The head, neck and chest were normal. In the right lower quadrant of the abdomen, there is a cystic-feeling tumor mass which is nontender, or only slightly so, slightly movable, does not apparently reach the anterior abdominal wall and lies above the brim of the pelvis. The right kidney is just palpable to deep palpation and is not tender. The left kidney, liver, gallbladder and spleen are not palpably enlarged or tender. Pelvic examination reveals no palpable abnormalities, the mass lies above pelvic palpation. Hematology on January 24, 1944: Hemoglobin 100 per cent, R.B.C. 4.8 million; W.B.C. 7300, P.M.N. 73, S.L. 22, monocytes 4, Kolmer and Kahn negative. Urinalysis, S.G. 1.005, albumin 0, sugar 0, casts 0, pus 0, red cells 0. Barium enema of the colon showed that it filled readily and presented no evidence of intrinsic organic lesion. The palpable mass in the right lower quadrant of the abdomen produces a compression and displacement deformity of the distal limb of the hepatic flexure and of the right side of the transverse colon; these segments of the colon are quite firmly attached to the mass, and this portion of the colon takes a course around the lower margin of the mass. Palpation elicits no tenderness over the colon or in the region of the palpable mass. The terminal ileum and appendix are not filled during the period of fluoroscopy. Retrograde pyelogram: Opaque material injected through catheters inserted into both ureters demonstrates normal outlines of the left calices, renal pelvis and ureter. The left kidney outline is normal in size, shape and position. The right kidney is normal in size; it occupies a low and rotated position and there is a moderate right pyelectasis. The right ureter is deviated sharply toward the left; the apex of this displacement curve is at the level of the lumbosacral joint and in this segment, the ureter deviation is evidently produced by the same palpable mass which produces displacement of the colon, in the previous barium enema examination. *Clinical Diagnosis:* Retroperitoneal cyst.

*Operation.*—A long right rectus incision disclosed a cyst which lay behind the terminal ileum and cecum and which had displaced the ureter medially and the cecum laterally and anteriorly (Fig. 1). The gallbladder, appendix and the pelvic organs were normal. The transverse colon was adherent to the cystic mass. The posterior peritoneum was divided lateral to the cecum and transversely below the terminal ileum for a distance of about five inches. The cyst, which was about the size of a grapefruit, then presented. By combination of sharp and blunt dissection, applying hemostats to the cut peritoneal edge for traction, it was possible to enucleate the cyst and it was not ruptured until almost completely removed (Fig. 2). It was filled with clear, brownish-yellow fluid. Bleeders were stopped by packing and ligature. The appendix was then removed, and the abdomen closed. The convalescence was uneventful.



FIG. 1.—Appearance of cyst after retracting transverse colon.

*Pathologic Examination.*—*Microscopic:* Dr. John D. McGovern: Multiple sections through the thickened area in the cyst reveals in one area a diffuse irregular anastomosing series of tiny cleft-like and well-formed channels lined by typical endothelial cells. Scattered foci of lymphocytes and monocytes are interspersed throughout this area and the large cyst. The lining is composed for the most part of a well-defined zone of collagenous connective tissue interspersed with irregular short bundles of a more deeply eosinophilic-staining material tending to produce elongated convolutional stria-like forms in the wall. At one point in the section the cyst is in direct continuity with a large area of typical angioma and the vessels contain occasional blood cells as well as precipitated lymph but the majority of the channels are truly without content. *Pathologic Diagnosis:* Retroperitoneal massive cystic lymphangioma.

This case is rather typical in that the patient was an adult female, the tumor was on the right side, the history and physical findings were characteristic, the size of the mass is about that usually encountered in previous case reports, and roentgenologic studies presented the characteristic appearances. Comparing this case with other case reports in the literature it might almost

be stated that this condition represents a fairly well-defined clinical entity as far as the history, signs, symptoms and treatment are concerned. The difficulty arises when one attempts to classify these cysts embryologically and to ascertain their incidence statistically by type.

Handfield Jones, whose article on this subject is the most widely quoted, and is generally regarded as a classic, gives the following classes of cysts. (I have changed his order to fit this paper.)

(1) Cysts of urogenital origin.
(2) Teratomatous or dermoid cysts.
(3) Lymphatic cysts.
(4) Cysts of mesocolic origin.
(5) Traumatic blood cysts.
(6) Paracytic cysts.
(7) Developmental cysts in full-formed kidney or pancreas.



FIG. 2.—Dissection of cyst half completed, ureter being freed.

On the last three classes of cysts this paper has no comment and Handfield Jones mentions them simply as of interest from the diagnostic point.

Standard pathology texts[16] give the incidence of cystic retroperitoneal tumors as being much lower than solid retroperitoneal tumors. Kretschmer and Hibbs[17] quote Gobell's[8] 1901 collected report of 101 retroperitoneal tumors of which 12 were retroperitoneal cysts. Frank[5] reviewed the literature between 1925 and 1936 and collected 107 cases of which eight were cysts. These included two lymphangiomas, two lymph cysts, two sanguineous cysts, one serous cyst and one hemangio-endothelioma (all recovered). The majority of these tumors were mesodermal in origin. There were also ten teratomas in his list, of which five recovered. Concerning the relative frequency of retroperi-
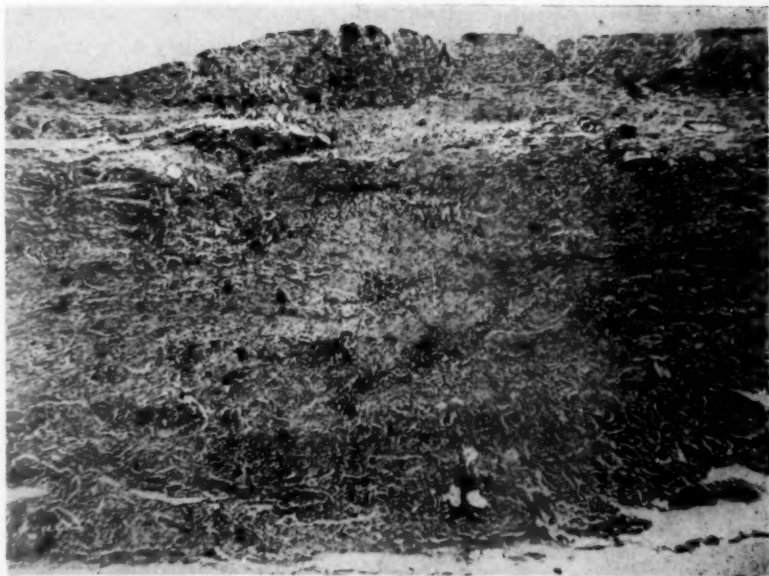
FIG. 3A.—Low power photomicrograph of cyst wall. (Thickest area).
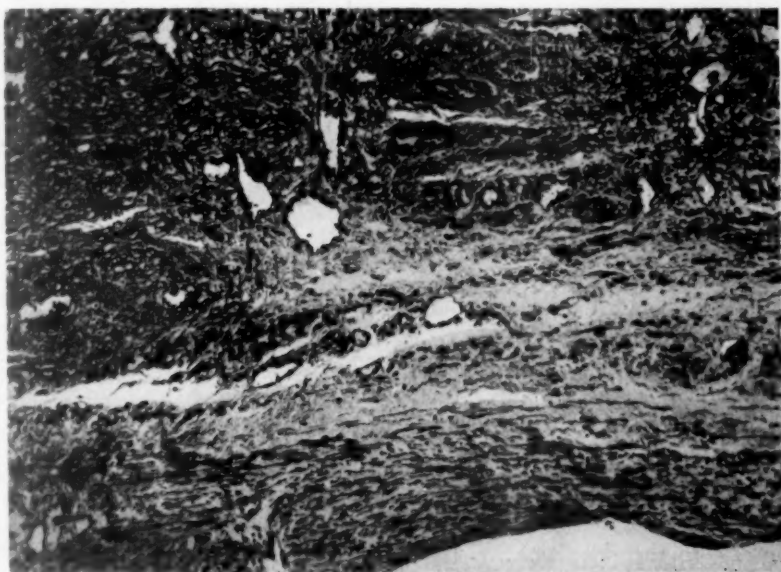


FIG. 3B.—Medium power photomicrograph of cyst wall. (Thickest area).

toneal *versus* mesenteric and omental cysts, Gerster[7] states that there are between 450 and 500 case reports on the latter and only 18 on the former.

According to Hinman, Gibson and Kutzmann[13] nearly all cystic retroperitoneal tumors have their origin from fetal renal elements. This view is supported by Maury,[22] and by Jacquot and Fairise.[15] Maury's case had tubules and glomeruli in the wall and a ureter-like tubular structure attached to it. Jacquot and Fairise' case also had recognizable renal elements in its wall and was situated between the layers of the descending mesocolon. This type of cyst was first described by Roth[29] in 1881. Hinman, *et al.*, state that "it is highly probable that a great variety of cystic and solid neoplasms of the retroperitoneal
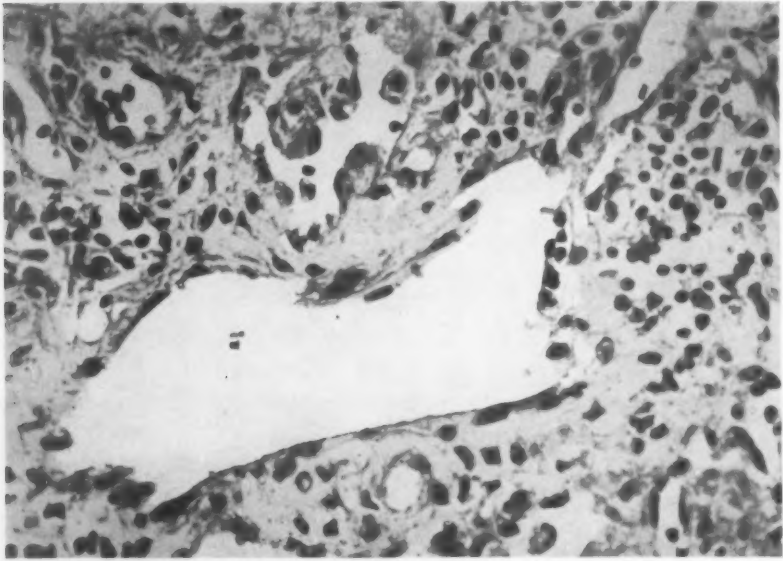


FIG. 3C.—High power photomicrograph of cyst wall. (Thickest area).

space in relation to the adrenal, kidney, broad ligament, spermatic cord, epididymis and possibly the testicle have their origin in wolffian body remnants." In support of this theory is the frequency of the condition in women where the mullerian duct makes up the generative tract and the wolffian body exists almost entirely as an atrophic unutilized condition. On the other hand, Hinman, *et al.*, quoting Maury, state that only five cases with primitive glomeruli and renal tubules in the wall are reported in the American literature. Their assumption is that the variety of findings, microscopically, in the wall of the cyst is due to the neoplasm arising out of one of the many portions of the wolffian body.

Closely related to cysts of wolffian body origin, and often considered as of the same type, are cysts arising from the cells of the genital ridge which lies just lateral to the wolffian body. These cysts, when characteristic, assume the

appearance presented by Stewart's[27] case, which was described as a unilocular compound cystic ovarian adenoma, four and one-half inches in diameter, situated on the outer side of the ascending colon. Stewart's conjecture poses the possibility that these cysts are distant relatives of retroperitoneal teratomas and dermoids of the ovary, the common ancestor being a totipotential sex cell which becomes sequestrated on its course from the morula to the genital ridge and later in adult life assumes independent growth qualities.

This view is more or less accepted by Lahey and Eckerson[18] who reported two cases of this type in 1934. They state that "mesenteric, omental, and retroperitoneal cysts must actually be grouped in the same category since the mesenteric or omental variety are merely an anterior extensive or inclusion of those originally retroperitoneal." The distinction, they go on to point out, is based on clinical signs while pathologically and embryologically, the cysts are alike. They suggest that since the cysts spring from one of the three germinal layers, those from the ectodermal and endodermal elements may be classed as dermoids and those of mesodermal origin called mesodermoids. Of Lahey and Eckerson's two cases, one was retrocecal and no microscopic report is appended. The other was reported as a simple cyst of the ovary and lay lateral to the descending colon.

Typical retroperitoneal teratomas are, as noted in Frank's review of the literature, at least as common as all other retroperitoneal cysts put together, but retroperitoneal dermoids are less common. Handfield Jones includes three cases in his review, these usually contained sebaceous material and hair.

Although there are a number of cases of chylous and nondescript lymphatic cysts reported in the literature, there are, or were according to Kretschmer and Hibbs, only five cases of typical retroperitoneal lymphangiomas, all on the right side, reported up to 1934 (two children and three adults). The view is supported by Ingraham and Nelson[14] who, in 1939, reported the case of a woman with a large cystic midline lymphangioma of the retroperitoneal space. They consider their case to be the sixth in the literature. While these authors quote McFadden,[25] and Makins,[21] as being of the opinion that many of the reported mesenteric and retroperitoneal cysts are lymphangiomas, they prefer not to accept this opinion.

Unfortunately, many of the earlier reports on so-called "chyle cysts" were based on the finding of a milky contents within these cysts rather than in accurate study of the cyst wall. Gerster, who made an extensive study of this subject, points out that chyle and lymph are indistinguishable grossly, and that studies of the fat content from lymph fistulae from the lower extremities have shown variations almost identical with chyle itself (from 0.6 to 47 per cent). He also quotes Volkmann[30] as having observed a chyle-containing cystic lymphangioma in the neck.

Hadley,[9] in 1916, pointed out that retroperitoneal lymphatic or chylous cysts are probably related to hygromata in the neck and are derived from one of the four primitive lymphatic sacs. The principal objection to this theory is that most of the abdominal cystic lymphangiomata reported have been in adults

while most hygromata of the neck are in children. In favor of this condition being a separate entity from wolffian body cysts is that the reported cases occur almost as often in males as females and while some of these cysts may be indistinguishable from some of the wolffian variety, some, at least, have quite definite characteristics of their own. A typical cystic lymphangioma has walls composed of connective tissue with numerous endothelial-lined lymph spaces which in some areas show cavernous development. Besides connective tissue, smooth muscle cells are present and more or less lymphoid infiltration. The cyst may have an endothelial lining or it may be absent. The contents may be serous or chylous and bloody if traumatized. No connection with nearby lymphatics is necessary.

Some of these cysts apparently arise from degenerating or regressive changes in cavernous lymphangiomas. Since Gerster's report, another case has been reported in 1942 by Lee.[20] Lee presents an ingenious hypothesis for the origin of chylous cysts: On the basis of a small effusion following trauma there is an ingrowth of endothelial cells and a cyst is formed by a reversed flow of chyle into this space.

TABLE I

ADDITIONAL CASE REPORTS NOT PREVIOUSLY SUMMARIZED

| Author | Sex | Age | Type | Size | Location |
|---|---|---|---|---|---|
| 1. Barthels[9] | F. | 44 | Lymphatic | Child's fist | Midline |
| 2. Corniology[4] | F. | 35 | Parchment-thin wall lined with calciform cells. | Infant's head | Retrocecal |
| 3. Forster[6] | F. | 36 | Wolffian type lined columnar epithelium. | Diameter 12-15 cm. | Connected to left kidney |
| 4. Lawen & Biebl[19] | F. | 18 | Wolffian type with glomeruli in wall. | 30 cm. long | Attached to right renal vessels |
| 5. Rosenfeld[26] | F. | 28 | Exceedingly thin lining, isolated epithelial cells and leukocytes. | Goose egg | Retrosigmoidal |

Handfield Jones distinguishes another type of cyst, which he calls mesocolic in origin, formed by imperfect fusion of the layers of the peritoneum. This cyst is found only in the area between the ascending and descending colon and below the transverse mesocolon and it always lies anterior to the spermatic or ovarian vessels. These cysts have a thin fibrous wall and a delicate flattened lining. He describes one case of this type which "is either mesocolic or lymphatic in origin." In perusing the literature, I have been unable to find any recorded cases which fulfilled these characteristics unless it be that of Wilson,[32] described in 1929, and Wilson is quite doubtful about the origin in his case.

From the foregoing review it seems apparent that there are actually two general types of primary developmental retroperitoneal cysts, the distinction between the two being as follows: One type is that derived from ectodermal (or perhaps of entodermal) elements, the wolffian body or genital ridge or a more primitive cell, and shows in its wall epithelial elements. This cyst usually occurs in women and occupies a lateral position. The second type is derived from mesodermal, or lymphatic elements and occurs in any age-group and either sex, and may have either a midline or a lateral position. As to the

incidence of either one of these types of cysts, one can only speculate. In addition to the 18 or 20 cases of lymph cysts collected by Gerster and the five wolffian body cysts reported by Hinman, *et al.*, there are Lahey's and Eckerson's two cases and others mentioned here, and I have been able to find at least three more wolffian types and two lymphatic in the literature not recorded in these summaries (Table I). . . . Incomplete references to the incidence of this condition are common. Hinman, *et al.*, state "the literature abounds with reports of cysts which are considered as being of wolffian origin—." Whipple,[31] discussing Gerster's paper, infers that he has had several cases. Barney,[1] in 1925, was able to find five cases in the records of the Massachusetts General Hospital and makes the statement that the tumors are more frequent in women than men. Stone,[28] discussing Barney's paper, remarks that he has had three or four cases in children. Hawthorne[12] stated that he had operated upon two patients for retroperitoneal cysts.

Regardless of their origin, the walls of these cysts are usually described as having three layers, microscopically : An outer connective tissue layer ; a middle lymphoid layer ; and an inner layer lined with flattened cells. At times these cells may assume columnar form and at other times they are so flattened as to be absent or endothelial in character. The presence of ovarian elements, adenomas or malignancies, skin, hair or lymphoid elements, *etc.*, is necessary to make an exact diagnosis. Except for dermoid types and cysts which have undergone inflammatory or malignant changes, the walls are so thin that they are often ruptured on removal. Most of the reported cases have, like the author's case, been found on the right side, that is retrocecally rather than retrosigmoidally.

The general group of symptoms noted in all these tumors is that of inconvenience, discomfort and pressure, incident to size. As a rule they are painless because they are slow growing and the function of adjacent structures is not impaired. General or local enlargement of the abdomen in conjunction with a feeling of discomfort is the most usual complaint. Other symptoms include anorexia, pain and dyspnea, all noted in the larger-sized tumors accompanied by weight loss. Infection occurring in these cysts is apparently of unusual occurrence, and presents the signs of local tumor with sepsis and severe pain.

The diagnosis of retroperitoneal cysts is made by a process of eliminating other possible tumors. The importance of pyelography and the barium enema in the diagnosis of retroperitoneal cysts has been pointed out by Lahey, *et al*. By these procedures, the correct diagnosis was made in the first case reported. The condition is to be suspected in a patient who has an asymptomatic, rounded, rather immovable cystic-feeling tumor in the right or left lateral abdomen. Disease of the kidneys, ureter or colon is ruled out roentgenologically ; mesenteric cyst, according to Moynihan,[24] is generally near the umbilicus and very mobile ; pancreatic cysts present in the upper abdomen and lie behind the transverse colon until quite large, and roentgenograms of the duodenum show elongation of the duodenal loop. Cysts arising from the adrenal, kidney, pan-

creas or the intestine are always to be ruled out in the differential diagnosis. Although these are also retroperitoneal cysts, they are not to be confused with the true primary retroperitoneal cysts under consideration above. A retroperitoneal cyst may also simulate a high-lying ovarian cyst, and be so diagnosed preoperatively.

The treatment of this condition is entirely surgical[3] and the uncomplicated cyst becomes a problem to the surgeon only because of its intimate relation to the great vessels and the ureter. By making a vertical incision in the peritoneum lateral to the cecum and extending this transversely across the brim of the pelvis and displacing the colon upward as well as medially, one can approach the ureter and great vessels and keep them under direct visualization during the process of removing the cyst. A little care in handling the mesentary of the bowel prevents any bleeding and, providing the field is kept dry, no difficulty should be encountered in avoiding the ureter and the great vessels. The cysts have a tendency to rupture during removal as the walls are very thin. This accident has no effect on the outcome of the operation but makes it more difficult to determine whether the entire cyst has been removed or not. Occasionally, marsupialization of the cyst wall may be necessary in cases in which the patient is a poor surgical risk or in complicated cases. This procedure will effect a cure in a chylous cyst.

The prognosis with removal of these cysts is excellent. Occasionally the cystadenomas undergo malignant changes, and Harrington and Ganshorn[11] report a case of a malignant cystic hemangio-endothelioma lying retroperitoneally, resulting in death of the patient.

## SUMMARY

A discussion of the various theories for the origin of primary retroperitoneal cysts has been given, together with the accepted methods of diagnosis, treatment and a report of a personal case.

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# A STUDY OF THE RESULTS OF THE SURGICAL TREATMENT OF VARICOSE VEINS

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Despite the many recent reports concerning the surgical treatment of varicose veins, it is difficult to find large series in which end-results after an adequate period of follow-up are given. Even more unusual are groups of cases in which comparisons are made between various types of operative procedure employed under similar conditions. Among the many competent and experienced authors there seems to be no general agreement on the operation offering the best chance of a cure of this very common disorder.

In 1942, Moore and Knapp[1] reviewed 121 cases of varicose veins from the Surgical Department of the New York Hospital. We present a reconsideration of their findings on the basis of a larger series of cases and, in addition, a study of factors which they did not discuss. To accomplish this we have reviewed all cases of varicose veins treated by operation between 1940 and 1944, to obtain information concerning physical findings, the type of operation employed, duration of hospitalization, number of postoperative injections required to give satisfactory results and the ultimate outcome, as determined by surgeons examining the patients in the Hospital clinic. Recent reports of the surgical treatment of varicose veins from other clinics have been reviewed.

The lack of proof that there is any one method which is superior to others in the treatment of varicose veins is demonstrated on our service by the simultaneous use of several operative procedures by surgeons on the three Services— men with the same relative ability and experience. During the past few years each of these three subdivisions of the Surgical Department has employed, almost exclusively, one of the three more common operative procedures—high saphenous ligation; multiple ligation; or stripping of the vein—without regard to the severity of the varicosities. It is believed that this nonselective factor adds considerably to the value of this study. The majority of retrograde injections of sclerosing solutions were done in the first two years of the period studied.

Patients complaining of varicose veins are first seen in our Varicose Vein Clinic, where the majority are treated by injections. The cases requiring more than this therapy are admitted to the hospital the day before operation. Almost without exception these patients have incompetence of the internal saphenous valves, as shown by a Brodie-Trendelenburg test, and 65 per cent were found to have incompetence of the communicating vessels as well. None gave evidence of obstruction of the deep veins by Perthe's test or modifications of this test.

The operations were carried out under local anesthesia by the resident staff, and consisted of five types of procedure: (1) High ligation of the internal

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saphenous at its junction with the femoral vein, following a technic described in the earlier paper from this clinic;[1] care was exercised to divide all collaterals of the upper portion of the vein and to remove a segment of 4 to 6 cm.; (2) high ligation of the saphenous vein at its junction with the femoral vein as in (1), plus multiple interruptions by ligation and division of the vein along its course, requiring three to seven incisions and averaging four; (3) high ligation of the vein as in (1), plus extirpation of a portion of the internal saphenous vein by means of the Mayo stripper. Two or three superficial incisions in the thigh were made along the course of the vein to secure and divide large collaterals and perforators; (4) high ligation as in (1), and retrograde injection of a sclerosing agent into the distal vein. In almost one-half of this group of cases the internal saphenous vein was also divided in the lower thigh and the distal segment injected. Five per cent sodium morrhuate was most often employed, usually injected by syringe through an urethral catheter as the catheter was withdrawn from the vein; (5) high ligation as in (1), and excision of a prominent varix in the lower thigh or calf.

Postoperatively, to occlude the remaining superficial venous circulation, the leg was immediately wrapped with three or four semielastic bandages applied while the foot is maintained in an elevated position, and reaching from groin to foot. The patients are ambulatory on the afternoon of the day of operation and, if possible, discharged from the hospital the next day. Sutures are removed in the Minor Surgery Clinic. Whenever indicated, the patients are referred to the Varicose Vein Clinic for the injection of sclerosing agents, and they are seen in the Follow-up Clinic at intervals of six and 12 months.

*Results.*—Of the 365 consecutive cases reviewed, 288 were followed for at least one year, the average period being 18 months. Thus, we have followed 80 per cent of our cases long enough to show most of the poor results due to failure of the operative procedure. Moore and Knapp[1] indicated that beyond one year there is little change in the comparative results. We have repeated their method of determining this fact in Table VI and find no significant relative change in operative results as the follow-up period is lengthened (Table VI).

Of the 288 cases with adequate follow-up, 124 were treated unilaterally, while 164 required bilateral operations; making a total of 452 extremities which form the basis of this study. The percentage of bilateral involvement of 56, agrees with Steubner's[2] reported 52 per cent. The right extremity was affected in 51 per cent, the left in 49 per cent of the total. Ochsner,[3] McPheeters,[4] and Steubner[2] also failed to show predilection for either leg.

Females predominated, comprising 70 per cent of our series. This ratio of 3 to 1 is noted by McPheeters and by Bernstein;[4] Ochsner and Mahorner's series showed a larger proportion of women, but their cases included a large number of females in whom pregnancy and varicosities coexisted. In our series of cases 70 of the 200 women gave pregnancy as the inciting cause of the condition.

The average age of the patients was 46.5 years. Ochsner's nonpregnant patients averaged 48.4 years; McPheeters reported the highest incidence of varicose veins in the sixth decade.[3, 4]

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The results of operation and postoperative sclerosing injections in our cases are classified in four groups: (1) Excellent, which implies absence of symptoms and absence of significant varicosities; (b) good, which denotes marked improvement but with the presence of minor complaints or small varicosities; (3) improved, showing definite improvement but with symptoms and moderate varicose veins; and (4) poor, showing little or no improvement, development of ulcers or need of further operative treatment.

Finally, because it is realized that any classification of results of treatment must be more or less arbitrary and subject to variables on the part of the patient and examining surgeon, the good and excellent results are combined as satisfactory and the improved and poor as unsatisfactory.

In Table I the results are classified according to the operative procedure. Seventy-nine per cent of the whole series were found to have been satisfactorily treated with the best results obtained by multiple ligation, high ligation with retrograde injection, and stripping, in the order named (Table I).

TABLE I

| | | Results* | | | | | |
|---|---|---|---|---|---|---|---|
| | | Unsatisfactory | | | Satisfactory | | |
| Operative Procedure | No. Cases | Poor % | Improved % | Total % | Good % | Excellent % | Total % |
| High ligation.......... | 103 | 7 | 24 | 31 | 36 | 33 | 69 |
| Multiple ligation....... | 121 | 5 | 7 | 12 | 48 | 40 | 88 |
| High ligation and retro- grade injection....... | 103 | 7 | 8 | 15 | 42 | 43 | 85 |
| Stripping.............. | 104 | 2 | 17 | 19 | 35 | 46 | 81 |
| Ligation and excision... | 21 | 10 | 19 | 29 | 38 | 33 | 71 |
| Total.............. | 452 | | | 21% | | | 79% |

* This shows percentages of satisfactory and unsatisfactory results obtained by the various procedures. Multiple ligation, high ligation with retrograde injection, and stripping, in the order named, gave the best results, while high ligation alone produced relatively unsatisfactory results.

Table II gives the average number of days of hospitalization required for each procedure. It is customary to discharge patients as soon as possible after operation because of the shortage of beds, and because it is felt that an early return to normal activity is a good prophylaxis against pulmonary embolism. Prolonged hospitalization, therefore, usually signifies the occurrence of complications, or the unwillingness of the patient to leave the hospital because of

TABLE II

| Procedure | Average Days Hospitalization* |
|---|---|
| High ligation.................................... | 3.6 |
| Multiple ligation................................ | 3.8 |
| High ligation and retrograde injection.............. | 4.4 |
| Stripping....................................... | 4.5 |
| Ligation and excision............................ | 4.4 |

* This shows the average hospitalization in days for each operations. It reveals that the more extensive procedures were followed by longer hospitalization.

discomfort. The table offers some information on the degree of pain suffered after the different procedures. As might be expected, the simplest operations—high ligation and multiple interruption—were followed by a shorter stay in the hospital than were stripping and retrograde injection, both of which may produce painful extremities (Table II).

Table III presents the average number of postoperative sclerosing injections required to give satisfactory results following each operation (Table III).

TABLE III

| Operative Procedure | Average Number of Injections* |
|---|---|
| High ligation | 4.3 |
| Multiple ligation | 3.4 |
| High ligation and retrograde injection | 2.0 |
| Stripping | 3.0 |
| Ligation and excision | 3.6 |

* Average number of postoperative injections following each of the procedures. Fewer injections were required after retrograde injection, stripping and multiple ligations.

The postoperative complications—phlebitis, infection of the wound, and a questionable instance of pulmonary embolism—are presented in Table IV. It will be seen that multiple ligation was followed by the largest number of complications, but, for the most part, these were minimal wound infections or failure of all incisions properly to heal at once. One case required readmission

TABLE IV

| Operative Procedure | Complications* |
|---|---|
| High ligation | 1 hemorrhage requiring reopening of the wound |
| Multiple ligation | 6 superficial wound infections or delayed healing |
| High ligation and retrograde injection | 1 severe bilateral phlebitis of internal saphenous |
| | 1 superficial phlebitis |
| Stripping | 1 hematoma of wound |
| | 1 superficial phlebitis |
| | 2 superficial wound infections |
| | 1 questionable pulmonary embolism† |

* Complications following multiple ligation were more numerous than after other procedures but more severe after retrograde injection. There were no fatalities.
† Diagnosis not verified by examination.

for three days, while the others were treated without difficulty in the Minor Surgery Clinic. The most serious complication was a painful bilateral phlebitis of the internal saphenous system following retrograde injection of 5 per cent sodium morrhuate. This patient required a total of 15 days' hospitalization.

In contrast to the earlier report of cases from this hospital which included two deaths from massive pulmonary infarction following high ligation and excision, this series had no deaths. An incident, suggestive of pulmonary embolism following a stripping operation, was reported to the clinic, but this diagnosis could not be confirmed by examination.

### SUMMARY AND DISCUSSION

On the basis of the results obtained in the cases studied, it would seem that any operation which combines high ligation at the saphenofemoral junction with the addition of multiple interruptions of the saphenous vein, stripping of the vein, or retrograde injection of a sclerosing solution will give from 80 to 90 per cent satisfactory results.

The results of multiple ligation were slightly better than those following the other procedures but the higher incidence of wound infection and poor wound healing associated with it are undesirable. These complications of the operation probably are due to the fact that more incisions are required and that a larger area of the leg must be exposed at operation, hence, draping can be less precise. It is believed that greater care in technic might eliminate this factor.

Table III, giving the number of postoperative injections following each procedure, indicates that to sclerose isolated segments resulting from multiple interruptions, necessitates a larger number of postoperative injections than are needed after operations which remove the vein by stripping or obliterates it by injection at the time of operation. However, since multiple ligation is a simple procedure it should not carry the same risk of embolism which radical extirpation of the vein or the injection of sclerosing solutions do.

Extirpation of the saphenous vein with the Mayo stripper gave good results in a high percentage of cases. Since, in this procedure, the vein actually is removed and all communicators severed, these satisfactory results can be expected. That they were not better than those following other operations may be due to the fact that the vein generally was stripped to just below the knee and incompetent communicators with the external saphenous or the deep veins of the calf were not adequately treated. If the operation is used, the stripping probably should be continued down to the ankle, as recently described by Hodge,[6] or combined with multiple ligations in the calf. Ochsner and Mahorner, in their monograph,[4] expressed fear of a high incidence of pulmonary infarction following any attempt at extirpation—a reasonable consideration not borne out by experience. The only case with symptoms suggestive of embolism, however, followed this procedure. Stripping the saphenous vein under local anesthesia usually causes the patient great discomfort and general anesthesia prevents their early mobilization.

High ligation with retrograde injection also was effective, and following this procedure, the smallest number of postoperative injections were required to obtain satisfactory results. This operation has been recommended by many experienced surgeons and has gained wide acceptance. Ochsner and Mahorner[4] consider it the procedure of choice when combined with low ligation in cases with incompetent communicators. From the experience with 2,582 ligations of varicose veins, McPheeters[5] concludes that the operation gives uniformly good results. In 1942, a series of reports from the Mayo Clinic, by Waugh and Heyerdale, and associates,[7, 8] recommend it as the procedure of choice. Pratt[9] reports 90 per cent and Sears[10] 81 per cent satisfactory results following this

operation. Lyall[11] describes the use of high ligation with retrograde injection in 200 private patients, and Pearce[12] reported a series from an Army hospital treated with good results.

Retrograde injection, however, has the disadvantage of the danger of producing painful and serious reactions. In 1942, Vaughn[13] found 44 cases of fatal pulmonary embolism following the injection therapy reported in the literature, and added one of his own. Atlas,[14] in 1943, called attention to the hazards of injecting sclerosing solutions either directly or retrograde, and expressed the opinion that injection at the time of operation was contraindi-

TABLE V

| Operative Procedure | Incompetent Communicators Results Unsatisfactory | Satisfactory | Competent Communicators Results Unsatisfactory | Satisfactory |
|---|---|---|---|---|
| High ligation* | 18 | 44 | 10 | 27 |
|  | 62 | | 37 | |
| Multiple ligation | 7 | 74 | 4 | 33 |
|  | 81 | | 37 | |
| Stripping | 14 | 50 | 5 | 30 |
|  | 64 | | 35 | |
| Ligation and retrograde injection | 8 | 50 | 4 | 38 |
|  | 58 | | 42 | |
| Ligation and excision | 1 | 11 | 3 | 5 |
|  | 12 | | 8 | |
| Total | 277 | | 159 | |

* Classification of results obtained with each procedure as related to the preoperative condition of the communicators; it shows the inadequate results achieved after high ligation in cases even without demonstrable incompetent communicators.

cated. In our series the operation was followed by serious complications in a few cases and, quite generally, by prolonged hospitalization. In recent years the method has been largely abandoned at the New York Hospital—not because of a great number of serious complications but because of the postoperative discomfort associated with the operation and because the results were not so satisfactory as following other procedures.

In our experience, simple high ligation has been relatively unsatisfactory. Only 69 per cent of the patients treated in this manner could be said to have satisfactory results. A higher percentage of good results could hardly be expected from a method which gives no consideration to the communicating vessels. With the added procedure of postoperative injections, the results might be expected to be adequate for an extremity in which no incompetence of the communicating vessels could be demonstrated. Our results offer evidence against this assumption. In Table V are presented the results according to the operation and the preoperative condition of the communicating vessels when this information was available (436 of 455 extremities). It will be seen

## TABLE VI

### PERIOD OF FOLLOW-UP

| Operative Procedure† | 1 year | | | | | 1.5 years | | | | | 2 years | | | | | 2.5 years | | | | | 3 years | | | | | 3.5 years | | | | | 4 years | | | | | 5 years | | | | | 6 years | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. | P* | I* | G* | E* | No. | P | I | G | E | No. | P | I | G | E | No. | P | I | G | E | No. | P | I | G | E | No. | P | I | G | E | No. | P | I | G | E | No. | P | I | G | E | No. | P | I | G | E |
| High ligation | (55) | 6 | 13 | 17 | 19 | (24) | 0 | 7 | 10 | 7 | (9) | 1 | 1 | 4 | 3 | (8) | 0 | 3 | 3 | 2 | (1) | 0 | 1 | 0 | 0 | (2) | 0 | 0 | 1 | 1 | (2) | 0 | 0 | 1 | 1 | (3) | 0 | 0 | 3 | 0 | (2) | 2 | 0 | 0 | 0 |
| Multiple ligation | (38) | 0 | 2 | 23 | 13 | (37) | 0 | 1 | 18 | 18 | (16) | 2 | 1 | 4 | 9 | (17) | 0 | 2 | 6 | 9 | (6) | 1 | 0 | 1 | 4 | (11) | 4 | 1 | 5 | 1 | (2) | 0 | 0 | 2 | 0 | (0) | 0 | 0 | 0 | 0 | (0) | 0 | 0 | 0 | 0 |
| Stripping | (38) | 0 | 5 | 13 | 20 | (17) | 0 | 3 | 5 | 9 | (24) | 2 | 2 | 8 | 12 | (7) | 0 | 1 | 1 | 5 | (4) | 0 | 3 | 1 | 0 | (2) | 0 | 0 | 1 | 1 | (0) | 0 | 0 | 0 | 0 | (6) | 0 | 0 | 4 | 2 | (0) | 0 | 0 | 0 | 0 |
| Ligation and retrograde injection | (29) | 0 | 1 | 11 | 17 | (23) | 6 | 2 | 14 | 1 | (26) | 5 | 2 | 12 | 7 | (8) | 1 | 0 | 6 | 1 | (10) | 0 | 3 | 2 | 5 | (4) | 0 | 0 | 0 | 4 | (4) | 0 | 0 | 2 | 2 | (0) | 0 | 0 | 0 | 0 | (0) | 0 | 0 | 0 | 0 |
| Ligation and excision | (9) | 0 | 1 | 4 | 4 | (4) | 0 | 0 | 2 | 2 | (3) | 0 | 0 | 1 | 2 | (0) | 0 | 0 | 0 | 0 | (0) | 0 | 0 | 0 | 0 | (1) | 0 | 1 | 0 | 0 | (1) | 0 | 0 | 0 | 1 | (0) | 0 | 0 | 0 | 0 | (0) | 0 | 0 | 0 | 0 |

\* P—poor; I—improved; G—good; E—excellent.

† Cases treated by each operation arranged according to result and length of follow-up, to show that there is no change in the comparative results of the operations as the follow-up period is lengthened.

that 10 of the 37 cases (27 per cent) without demonstrable incompetence of communicators, treated by high ligation, gave unsatisfactory results, while only four of the seven (11 per cent) treated by multiple ligation, five of 35 (14 per cent) subjected to stripping, and four of 38 (10 per cent) treated by ligation and retrograde injection were unsatisfactory. Further evidence can be deduced from the results in cases with proven incompetent communicators subjected to high ligation (29 per cent unsatisfactory), which were only slightly worse than those without such incompetence (27 per cent). Finally, high ligation with only one interruption—by excision of a varix in the thigh or calf—gives more satisfactory results than high ligation alone. It is believed that even when no incompetent communicators can be demonstrated at the time of operation, interruption of the saphenous at, or below, the usual site of the communicators should be carried out on the assumption that incompetence was not detected by the clinical tests or that the communicating vessels may become incompetent later. Any communication with an incompetent external saphenous vein should be given careful consideration, as has been emphasized by Heyerdale.[15]

### CONCLUSIONS

(1) High ligation of the saphenous vein combined with multiple ligations, retrograde injection or stripping of the vein have been

found to give between 80 and 90 per cent satisfactory results in 452 cases of varicose veins observed for one year or more after operation.

(2) Hospitalization was longest and degree of discomfort to the patient was greatest following retrograde injection or stripping; and least after high ligation or multiple ligations.

(3) Complications were more frequent after multiple ligation though the majority were not serious, and phlebitis occurred more often after retrograde injection. There were no proven cases of pulmonary embolism, and no deaths.

(4) Simple ligation with retrograde injection required the smallest number of postoperative sclerosing injections to attain satisfactory results.

(5) Multiple ligation, combining the advantages of a safe procedure easily performed under local anesthesia, with superior results is, in our experience, the operation of choice.

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# PERSISTENT OMPHALOMESENTERIC (VITELLINE) ARTERY CAUSING INTESTINAL OBSTRUCTION AND GANGRENE OF MECKEL'S DIVERTICULUM*

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AMONG THE RARER CONDITIONS which are encountered in surgery those which precipitate practical problems are especially worthy of consideration. Persistent omphalomesenteric, or vitelline, artery falls into this category. Its presence is one of the infrequent causes of intestinal obstruction. The literature contains only 16 cases in which a persistent omphalomesenteric artery caused symptoms, and, of this number, evidence of intestinal obstruction was found at operation or autopsy in 11 cases (69 per cent). In addition, six asymptomatic cases have been reported, making a total of 22 cases of persistent omphalomesenteric artery in the literature.

Of these 22 cases, a Meckel's diverticulum of the ileum was present in 13 (59 per cent). Of the 11 cases presenting evidence of intestinal obstruction at operation or autopsy, 10 (91 per cent) had a coexistent Meckel's diverticulum. This association is not surprising if we consider the origins and fates of these structures in the embryo.

## EMBRYOLOGY [1, 2, 4, 13, 18, 25, 26]

The yolk sac is demonstrable at the second week of intra-uterine life. The yolk sac and the primitive gut are connected to each other by the yolk-stalk, or vitelline (omphalomesenteric) duct. The part of the gut to which the omphalomesenteric duct is attached is the midgut; from it are derived the small intestine (except the first part of the duodenum), the cecum, the ascending colon and the transverse colon.

During the first weeks of embryonal development, the aorta is a paired structure (Fig. 1). From each portion a prominent vessel courses ventrally to the primitive gut and thence out along the yolk-stalk to reach the yolk sac. With the merging of the paired aorta into a single aorta the two main ventral branches merge and the resultant vessel comes to be the superior mesenteric artery (Figs. 2 and 3); or it may be postulated that in certain cases these ventral branches do not merge and that one of the large ventral branches grows while the other recedes, the developing one becoming the superior mesentery artery. If the other ventral branch does not recede completely but persists in an attenuated form it may be identified later as the persistent omphalomesenteric vessel (Fig. 4), at least that part running from the ileal mesentery to a Meckel's diverticulum or to the under surface of the umbilicus, or to both. However, this theory of formation may not be complete. Where the main ventral vessels have merged to one main trunk this single ventral

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artery reaches the forming midgut and the artery's continuation out along the vitelline duct is a paired one. At the time when the vitelline duct separates from the midgut (after six weeks) the yolk sac and the duct disappear. At this time, one, or more, of the vessels which ran along the vitelline duct from gut to yolk-sac may not disappear but persist and be labeled a persistent vitelline artery.

If the gut-end of the omphalomesenteric duct persists and remains in communication with the bowel it is designated a Meckel's diverticulum. This is found at 2 to 3 per cent of autopsies.

Persistence of the omphalomesenteric artery manifests itself as an adventitious, intra-abdominal, fibrous band (which may, or may not, contain a patulous vessel) covered by peritoneum. The persistent artery, in all but a few cases, is attached at each end (13 cases out of 22 reported, or 59 per cent). Usually one end is attached to the anterior abdominal wall and the other end is attached either to the ileal mesentery or to a Mackel's diverticulum. Less often, (seven cases, or 32 per cent) it connects a Meckel's diverticulum to the ileal mesentery. In a few cases, the cord is attached at only one end. In these
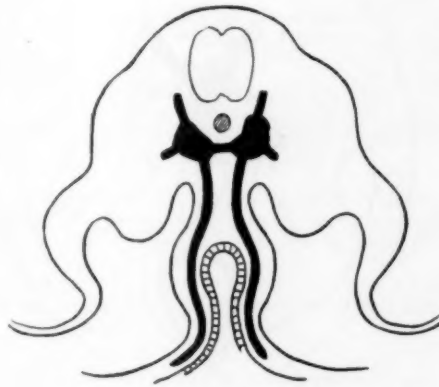


FIG. 1.—Cross-section of a human embryo at approximately two and one-half weeks. This shows paired aortae joining to become a single vessel. The two main ventral branches are shown going down to the forming midgut.

latter instances, both in infants, the unattached end hung harmlessly free in the abdomen, and gave no symptoms.

### LITERATURE AND CLINICAL CONSIDERATIONS (TABLE I)

The first cases on record were two reported by Sandifort,[20] in 1777. Meckel,[16] in 1809, reported a case, and was the first writer to suspect the true origin of this condition. Fitz,[8] in 1884, gave an excellent résumé of the cases reported up to that date, disproved the view that these fibrous bands were inflammatory in origin, and clearly described the manner in which they arose. Contemporary reports are those of Postoloff,[17] and of Smithy and Chamberlin,[24] in 1946.

The first symptomatic cases in the literature varied in age from four months to "old age." The youngest case of intestinal obstruction was one year old.[23] Of the six asymptomatic cases, only one was an adult.[5]

Three clinical pictures may be seen:

(1) *Acute Intestinal Obstruction;* with evidence of same at operation or autopsy. Eleven cases (69 per cent) were in this group.[6, 7, 8, 14, 15, 17, 20, 23] Survival of such a case has not been reported.

(2) *Recurrent Abdominal Pain;* occurring over periods of several months to many years. Four cases (25 per cent) were in this group.[3, 10, 22, 24] Pain was in the right lower quadrant, epigastrium or periumbilical area. Excision of the band resulted in cure in all cases.
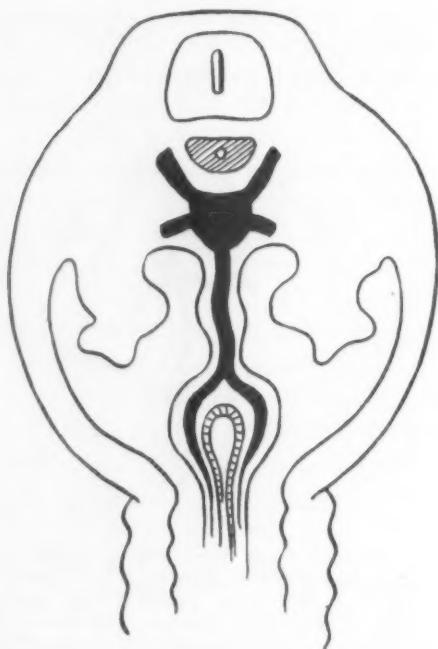


FIG. 2.—Cross-section of embryo at about five weeks. There is a single aorta and one main ventral branch, the other having merged, or regressed. The midgut is almost closed and the connection between it and the yolk-sac beyond is now a narrow tube. On each side of it branches of the principle ventral artery (especially the two main trunks) continue to the wall of the yolk sac. The midgut will close and the connection between it and the yolk-sac will regress.
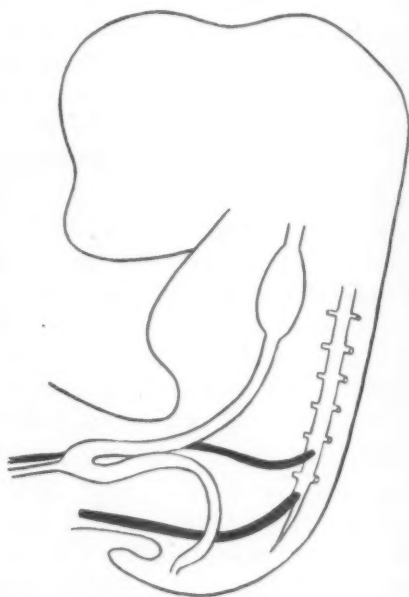
FIG. 3.—Sagittal section of embryo at about five and one-half weeks. The main ventral artery is seen coming from the aorta to the almost closed midgut. One branch of it is shown continuing along with the still-present vitelline duct. Shown below is one of the umbilical arteries arising further down the aorta and making its exit into what is to be the umbilical cord.

(3) *Intra-abdominal Hemorrhage:* Only one such case has been reported.[9] In a four-month-old infant, cauterization of granulation tissue at the umbilicus necessitated traction on the pedicle by which it was attached. Death resulted from intra-abdominal hemorrhage. Autopsy revealed a cord extending from the umbilicus to the ileal mesentery, the cord was attached to a branch of the superior mesenteric artery. Another nearby branch of the superior mesenteric artery had ruptured.

**Case Report.—No. 9555.** E. M., male, white, age three years, was admitted to the Nazareth Hospital, on June 22, 1946. The patient's mother stated that the child had suffered periumbilical pain and vomiting for three days. No symptoms referable to

TABLE I

COLLECTED CASES OF PERSISTENT VITELLINE ARTERY

| Author | Date | Sex | Age | Findings |
|---|---|---|---|---|
| Standifort[20] Case 1 | 1777 | ? | Adult | Seciform diverticulum, with blind extremity attached by tough cord to left side of cecum, forming noose to constrict intestine. Fatal intestinal strangulation. |
| Case 2 | 1777 | ? | ? | Diverticulum of ileum, adherent at tip to mesentery. Through ring thus formed, intestine had become strangulated. |
| Case 3 | 1793 | ? | Infant | "Appendix" arising from ileum, united at its end to upper part of mesentery by narrow strong thread. Asymptomatic. |
| Eschricht[6] | 1834 | F | "Old" | Meckel's diverticulum attached by persistent vitelline artery to ileal mesentery, forming loop which caused fatal strangulation of intestine. |
| Falk[7] | 1835 | ? | 20 yrs. | Persistent vitelline artery uniting free end of Meckel's diverticulum with ileal mesentery to form loop. Fatal intestinal strangulation. |
| King[14] Case 1 | 1843 | ? | 14 mos. | Patent Meckel's diverticulum adherent to umbilicus, forming enteric fistula. Adventitious cord connecting diverticulum to ileal mesentery compressed the ileum, causing fatal intestinal obstruction. |
| Case 2 | 1843 | ? | ? | Cord extending from base of Meckel's diverticulum to ileal mesentery, causing fatal intestinal obstruction. |
| Mahomed[15] | 1875 | M | 18 yrs. | Band extending from anterior abdominal wall midway between pubis and umbilicus, to ileal mesentery, acted as noose to cause fatal intestinal obstruction. Meckel's diverticulum present. |
| Fritz[8] Case 1 | 1884 | ? | 28 yrs. | (Warren Museum, Specimen No. 496, Improvement Collection) Diverticulum of ileum with cord proceeding from end of diverticulum to upper surface of mesentery. Through ring thus formed, intestines became strangulated, with fatal results. |
| Case 2 | 1884 | M | 21 yrs. | Diverticulum of ileum with tendinous cord proceeding from diverticular mesentery to umbilicus. Fatal intestinal strangulation. |
| Sheen[23] | 1916 | M | 1 yr. | E.T.L.: Umbilicus polypus excised and base cauterized. Death one week later of intestinal strangulation. Meckel's diverticulum attached to umbilicus by cord. Ileum herniated through hole in diverticular mesentery; strength of constricting cord of mesentery largely due to vessel transversing it. |
| Postoloff[17] | 1946 | M | 38 yrs. | Attacks of cramping abdominal pain for two years. Cord extending from umbilicus to ileal mesentery, causing fatal intestinal strangulation. No diverticulum. |
| Fraser and McCartney[9] | 1920 | ? | 4 mos. | Granulation tissue attached to pedicle in umbilicus. Actual cauterization performed, necessitating traction of pedicle, which caused rupture of branch of superior mesenteric artery in ileal mesentery with fatal intra-abdominal hemorrhage. Cord extending from umbilicus to ileal mesentery cord was attached to branch of superior mesenteric artery. No diverticulum. |
| Shaw[22] | 1925 | F | 43 yrs. | Right lower quadrant abdominal pain since childhood. Hysterectomy performed for vaginal bleeding; at operation, found band extending from ileal mesentery to anterior abdominal wall near right inguinal ring. Band transfixed omentum. No diverticulum. Cure followed excision of band. |

TABLE I *Continued*

COLLECTED CASES OF PERSISTENT VITELLINE ARTERY (Continued)

| Author | Date | Sex | Age | Findings |
|---|---|---|---|---|
| Gautier[10] | 1931 | M | 21 yrs. | Repeated attacks right lower abdominal pain. Persistent omphalomesenteric artery extended from umbilicus to ileal mesentery. No diverticulum. Excision of band resulted in cure. |
| Buchanan and Wapshaw[3] | 1940 | ? | 12 yrs. | Intermittent colicky pain in right lower quadrant and periumbilical area, with vomiting. Persistent vitelline artery extended from umbilicus to ileal mesentery. No diverticulum. No obstruction at operation. Excision of band resulted in cure. |
| Smithy and Chamberlin[24] | 1946 | M | 25 yrs. | Intermittent epigastric and periumbilical pain, with vomiting, for six months. Relieved by reclining. Fibrous cord extending from umbilicus to ileal mesentery. Cord looped over ileum to left of latter so as to support weight of terminal ileum and cecum when patient was erect. No diverticulum. No obstruction at time of operation. Excision of cord resulted in cure. |
| Derbes and Hoge[5] | 1937 | ? | Adult | Asymptomatic. Dissecting-room cadaver—death from tuberculosis. From free end of Meckel's diverticulum, cord extended to umbilicus. Patent omphalomesenteric vessels run along "mesenteric" border of diverticulum. At top of diverticulum, these were joined by branches from inferior epigastric vessels. From this anastomosis runs impervious arterial connection to right obliterated hypogastric artery. Two nonpatent vessels run inferiorly to fascia surrounding urachus on visceral end; omphalomesenteric vessels join ileal of superior mesenteric vessels. |
| Meckel[16] | 1809 | ? | Infant | Asymptomatic. Vessel unattached at one end. |
| Ruge[19] | 1877 | ? | Infant | Asymptomatic. Vessel unattached at one end. |
| Gesil[11] | 1938 | ? | New born | Asymptomatic. Death from intracranial hemorrhage. Cord attached to umbilicus and to mesentery. |
| Hyrtl[12] | 1870 | ? | ? | Asymptomatic. "Very fine thread—running from mesentery to side of peritoneum, where umbilical artery was lacking." |

the urinary tract were offered. There was no constipation nor diarrhea. Past medical history was essentially negative. The parents were in good health; one sibling was living and well.

Physical examination revealed a sturdy white male child showing obvious restlessness. Temp. 98.6° (R). Pulse 96. Respirations 22. There was moderate tenderness on deep palpation in the right lower quadrant of the abdomen. No distention, rigidity nor rebound tenderness were elicited. Peristaltic sounds were normal. Digital rectal examination was negative. *Laboratory Data:* R. B. C. 3,150,000, Hb. 71 per cent; W. B. C. 12,500, neut. 90 per cent, lymph. 10 per cent. Urinalysis: Neg.

Because of increasing restlessness, diagnostic spinal tap was performed six hours after admission; the findings were normal.

Twelve hours after admission, his temperature rose to 101.4° (R); pulse to 128; and respirations to 38. Examination then revealed abdominal distention, generalized rigidity and tenderness, most marked in the right lower quadrant. Peristaltic sounds could not be heard. The patient was prepared for surgery, and given 500 cc. of 5 per cent glucose in saline intravenously.

*Operation.*—Under nitrous oxide-ether anesthesia, a right pararectus incision was made (Fig. 5). On opening the peritoneum, there was seen a gangrenous, swollen Meckel's diverticulum of the ileum; the diverticulum was 7 cm. in length. There was also apparent a tough, rounded, taut adventitious cord, 3 cm. in diameter, proceeding from the umbilical area posteriorly and towards the right for a distance of 3 cm. to attach to the mesentery of the diverticulum, thence, after leaving the mesentery of Meckel's diverticulum, it proceeded for another 3 cm. to end in the base of the ileal mesentery.

The diverticulum itself was completely black, and there was torsion of its neck. It was presumed that the sac had looped itself through the opening between itself and the proximal portion of the persistent vitelline artery (that running from its own mesentery to the base of the ileal mesentery). A loop of ileum had slipped through the noose formed by the latter part of the cord and had become obstructed. The serosa of the obstructed bowel was injected
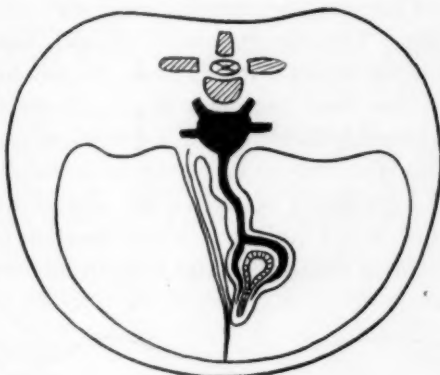


Fig. 4.—Schematic drawing of cross-section of embryo at about six and one-half weeks showing gut incompletely closed, a small pouch persisting where the vitelline duct led off. This is a Meckel's diverticulum. Along the side of the mesentery of the intestine the remains of one of the main ventral vessels runs out to the diverticulum and, thence, to the under surface of the abdominal wall. This is the persistent vitelline artery.

but viable. The intestine proximal to the obstructed loop was distended; that distal to the loop was collapsed. The vessel-containing cord was clamped, ligated and divided in four places, and removed in two sections. The Meckel's diverticulum was untwisted and resected. The abdomen was closed without drainage.

*Postoperative Course:* Four days postoperatively, the temperature suddenly rose from normal to 103.6 (R). The patient was restless; the abdomen distended and tympanitic. Penicillin 200,000 units i-m given every three hours. On the following day, the temperature dropped to normal and remained so; the abdominal distention was relieved. The patient was discharged in good condition on the 11th postoperative day. Seen six months following discharge; the patient was found to be in excellent condition, and without symptoms.

*Pathologic Report:* "(A & B) Club-shaped, sac-like piece of tissut, 7.2 cm. in length. Blind end is larger, and measured 2.8 cm. in diameter; the other end measured 1.9 cm. in diameter. Wall is thickened and covered with fibrin, and is dark purplish-red. On one side is a small vessel coursing along its middle, 3 cm. in length. Each end has a small catgut ligature, and is 2 to 3 mm. in diameter.

"(C) Wall, necrotic and purplish-red, and measures 3 to 4 mm.

"(D) Rounded, reddish-brown structure, 2.9 cm. long and 3 mm. in diameter, filled with coagulated blood. Catgut ligature on each end.

"Microscopic: (D) Zone of connective tissue; infiltrated with neutrophils. Numerous hyperemic capillaries are noted."

## SUMMARY

1. The embryology of the omphalomesenteric artery is presented. Persistent omphalomesenteric artery is explained on the basis of the failure of the primitive-paired main ventral arteries to fuse; one continues to develop

and becomes the superior mesentery artery, the other persists in an attenuated form. This theory would explain, most logically, those cases in which the residual artery extends from the mesentery of the ileum to a Meckel's diverticulum (and continues in some cases to the under surface of the umbilicus) or extends directly from the mesentery to the under surface of the umbilicus. This type truly deserves the name omphalomesenteric artery.

Persistence of one of the vessels which run along the vitelline duct, and which could have been a continuation of one of the pair of main ventral vessels or a continuation of the single fused main ventral vessel, would explain those cases which clinically present a persistent vessel or the remains thereof, running from the ileum or from a Meckel's diverticulum to the under surface of the umbilicus. Such a vessel seems better designated as a persistent vitelline artery.
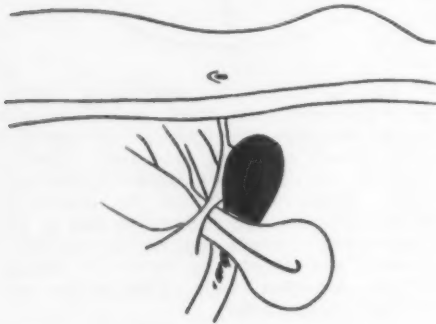


FIG. 5.—Illustrated are the conditions found at operation in the present case. The persistent remains of the vitelline artery, with its coverings, extends from the under surface of the umbilicus to the gangrenous Meckel's diverticulum, and, thence, to the mesentery of the ileum. Looping through the noose formed by this proximal portion is the segment of small bowel, which was incarcerated.

2. The literature of persistent omphalomesenteric arteries is reviewed, and the clinical significance of this condition is discussed.

3. A case of intestinal obstruction due to persistent omphalomesenteric artery is presented. The presentation of this case is of interest for the following reasons:

(a) The rarity of persistent omphalomesenteric artery.

(b) Survival has never previously been reported in such a case showing evidence of intestinal obstruction at operation.

(c) Gangrene of Meckel's diverticulum as a result of torsion of its neck contributed to, and maintained by, a taut persistent omphalomesenteric artery has not previously been described.

4. No characteristic set of signs and symptoms can be called pathognomonic of persistent vitelline artery. The symptoms vary with the complication produced. The important thing is to recognize the presence of an "acute" abdomen, and the diagnosis of the persistent vitelline artery is really only possible with the abdomen open. It is well to know, however, that it may be one of the underlying causes of intra-abdominal pathology, and that one may occasionally encounter it.

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# HOW LONG SHOULD AN EXTREMITY BE IMMOBILIZED AFTER NERVE SUTURE?*

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END-TO-END SUTURE of a nerve is hardly ever possible without the use of various procedures for overcoming gaps which result from the loss of substance of nerves or the retraction of their stumps. The methods commonly used for gaining length consist of the often extensive freeing of the nerve, rerouting or suturing it with the neighboring joints flexed. Even when these steps are taken it is sometimes necessary to introduce nerve grafts, but end-to-end suture is preferable to the use of grafts provided that this can be accomplished without great strain on the suture line. In those instances where joints must be flexed in order to bring nerve ends into apposition and remove tension from the suture line, the question arises as to how long the limb must be immobilized in the flexed position. There exists a considerable degree of difference with respect to practice in such cases. Groff and Houtz[1] have suggested a two-week period as adequate while Hambly[2] advocates immobilization of the extremity for a period of 9–12 weeks following nerve repair. The surprisingly high incidence of separation at the suture site of 7.5 per cent (44 out of a total of 604 nerve sutures) reported by Whitcomb[3] was probably to a large extent attributable to inadequate immobilization of the sutured nerve since in some cases "fairly rapid extension of the flexed joint as early as two weeks after operation" was carried out. It is apparent that the period of immobilization must be long enough to avoid rupture of the suture site when the joint is extended. On the other hand, one must avoid too prolonged fixation of the joint since the inevitable muscle atrophy and periarticular changes that ensue delay or even prevent recovery of function. Active and passive motion of the joint over which the sutured nerve passes must not be started before satisfactory healing of the suture line has occurred but it must not be delayed unnecessarily beyond this point. An attempt has been made in this study to resolve this apparent dilemma by the performance of a series of experiments upon rabbits and dogs. Microscopic studies of the process of healing at the suture line together with determinations of the tensile strength of the sutured nerve were made.

A previous attempt was made to settle this problem by Miller.[4] He carried

A                                            B



C

FIG. 1.—(A) Nerve sutured with plasma clot and removed four days after operation. Union of stumps has not occurred. (Hematoxylin and eosin, x 22.)

(B) Five-day-old sutured nerve. Streaming of cells across the suture site has occurred. (Hematoxylin and eosin, x 32.)

(C) Nerve sutured with plasma clot seven days before excision of specimen. Slight seepage of plasma into suture line has occurred and there has been cellular proliferation between the stumps. (Hematoxylin and eosin, x 20.)

out experiments in 11 dogs, suturing the sciatic nerve with silk or catgut. Tensile strength determinations were made of the suture site at the following intervals after operation: 1 week, in 3 dogs; 2 weeks, in 2; 3 weeks, in 2; 4 weeks, in 1; and 5 weeks, in 3 animals. Miller concluded that the strength of the suture line was "practically as great at the end of the third week as at the end of the fourth or fifth week." Comparisons of the strength of the suture line with the strength of the intact nerve were not made. Singer[5] showed that the tensile strength of the sciatic nerve of rabbits in which suture was accomplished by the use of fibrin film and thrombin, remained approximately constant during the first three postoperative days, but dropped by the fourth day to an average of 90 Gm. from an initial value of just over 100 Gm. After the fourth day it rose to an average of 338 Gm. on the sixth day and 625 Gm. on the tenth day. The results showed that "sufficient healing occurred by the end of the fifth or sixth day to ensure retention of the stumps without the aid of the suture material." Singer's studies were not carried beyond ten days after suture.

### METHOD

In our experiments both sciatic nerves in a series of 14 rabbits were exposed, severed and then sutured by the use of the autologous plasma clot technic.[6] Two of the three untwisted strands of No. 00 corticelli black silk were used as tension sutures to approximate the nerve ends and accurate apposition was achieved with the aid of plasma clot. The tension sutures were employed in order to avoid strain on the suture site during the unrestricted movements of the animal following recovery from the anesthetic. The animals were sacrificed at various intervals after operation, and 4–cm. segments of the nerve were removed (2 cm. to each side of the suture site). Also, 4–cm. segments of intact sciatic nerve were excised. The silk tension sutures were removed and tensile strength measurements were made of the suture site, the intact nerve, and of one of the withdrawn silk tension sutures from each nerve. For the purpose of microscopic study, the same technic of nerve suture was used upon the sciatic nerves of dogs, with the exception that tantalum wire (.003-inch in diameter), which causes less tissue reaction than silk,[6] was used as tension sutures. Observations were made upon several hundred such nerves at intervals ranging up to 18 months after operation. This material was prepared for study by a variety of histologic technics (hematoxylin and eosin, Laidlaw's connective tissue method, Gros-Bielschowski technic for axis cylinders, and osmic acid technic for myelin sheaths). The results of this study of nerve regeneration will be published later. For our present purpose, the observations upon this material concern the process of healing at the suture line with reference to restoration of its structural continuity.

The technic employed for the measurement of tensile strength was essentially that described previously.[7] Increasing increments of weights were applied until rupture of the nerve took place.

## OBSERVATIONS

Few monocytes and polymorphonuclear leukocytes appear within the plasma cuff as early as 24 to 48 hours after nerve suture, and an occasional fibroblast may be seen at this time. The fibroblasts increase in number and a
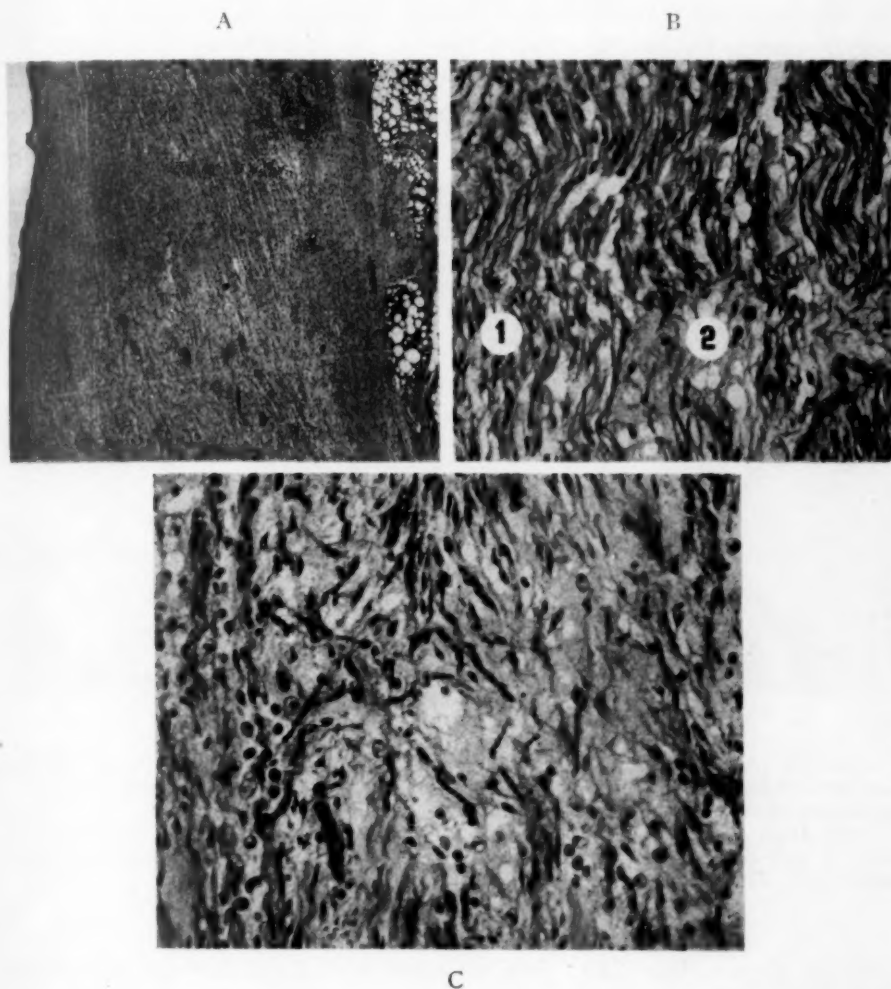
A                                              B



C

FIG. 2.—(A) Nerve sutured with plasma clot and removed nine days later. Incomplete union of the stumps has occurred. This is more apparent in (B) and (C) where macrophages as well as proliferating cells of the fibroblastic and schwannian types are seen. Cellular and fibrous continuity is seen in (B) at 1, but not at 2. Microphotographs taken from sections stained with hematoxylin and eosin, (A) x 20; (B) x 200; (C) x 200.

normal epineurium is reconstructed from the plasma sheath in seven to ten days. Within a period of two to three days after suture mild, degenerative, exudative and proliferative changes appear at the junction of the nerve stumps

Few polymorphonuclear leukocytes together with some monocytes and lipo-
phages appear at this time. These latter cell types may persist for several
weeks. Fibroblasts and Schwann cells proliferate and may frequently be seen
streaming out into a slight exudate between the nerve stumps. Although
Schwann cells are usually larger and present more oval nuclei than fibroblasts
the differentiation between these cells may be impossible without the aid of
special staining technics.[8]

As early as 3 to 5 days after suture, cells may be seen streaming across the
suture line (Fig. 1B), but occasionally signs of such cellular proliferation are



A          B
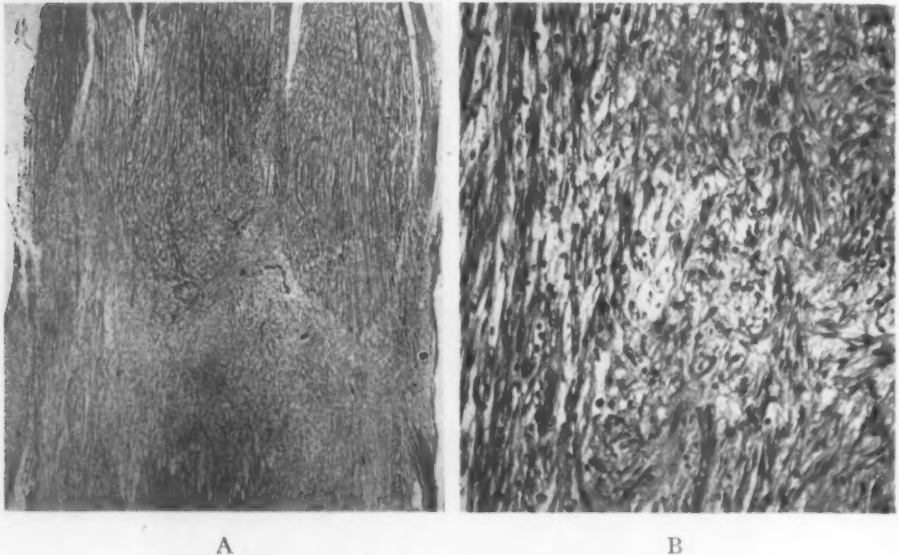
FIG. 3.—(A) Nerve sutured with plasma clot and removed 11 days later. Almost
complete cellular and fibroblastic continuity has occurred. (Laidlaw's lithium silver car-
bonate impregnation for connective tissue, x 20.)

(B) High power view of nerve seen in (A). Structural continuity of framework of
nerve is seen on the left but not on the right, where the cellular orientation is less
satisfactory. (Hematoxylin and eosin, x 150.)

strikingly absent (Fig. 1A). Sections taken nine days after operation have
shown structural continuity of schwannian and endoneurial sheaths, although
not uniformly in all cases (Fig. 2). In some nerves at this age, structural
continuity was seen at one portion of the suture line, whereas examination of
adjacent areas revealed the presence of a coagulum occupied by monocytes
and lymphocytes. This same variation in appearance of the suture line was
seen in specimens examined 11 days (Fig. 3), and to a less extent 14 days
after suture (Figs. 4 and 5). In some instances suture lines nine, 11 and 14
days old proved to be remarkably free from cellular infiltration (Fig. 5B). In
practically all cases of sutures 18 days or particularly three or more weeks old,
complete restoration of structural continuity has occurred (Figs. 6 and 7).

The growth of nerve fibers through the suture line may be demonstrated at this age.

At times, as a result of seepage of plasma into the nerve junction, or because of faulty apposition of nerve ends, Schwann cells, fibroblasts and connective tissue fibers become oriented transversely to the plane of the nerve. Although this is an undesirable occurrence because of the ensuing disorientation of nerve fibers at the suture line, the intrusion of a few drops of plasma at the suture line has been found to be compatible with satisfactory regeneration.



Fig. 4.—Nerve sutured with plasma clot and removed 14 days later. Restoration of continuity has occurred. (Hematoxylin and eosin, x 32.)

Examination of Table I tends to confirm the histologic observations, in that the suture site regained, or even exceeded, the strength of the intact sciatic nerve 19, or more, days after operation. It is of interest that in rabbits Nos. 5 and 12 (17- and 36-day-old nerves), in which the strength of the suture sites was considerably less than that of the intact nerves, the apposition at the suture sites was poor. In two animals (rabbits Nos. 3 and 4) the strength of the sutured nerves (13 days old) closely approximated that of the intact nerves. This is in keeping with the histologic observations which in some instances (Figs. 4 and 5A) showed structural continuity at this time. The degree of variation in tensile strength values of sutured nerves of a certain

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age corresponded to the histologic differences observed at the suture site at the same age approximately. The variations seemed to result from differences in the type of apposition obtained at the suture line. The nerves appeared to

A
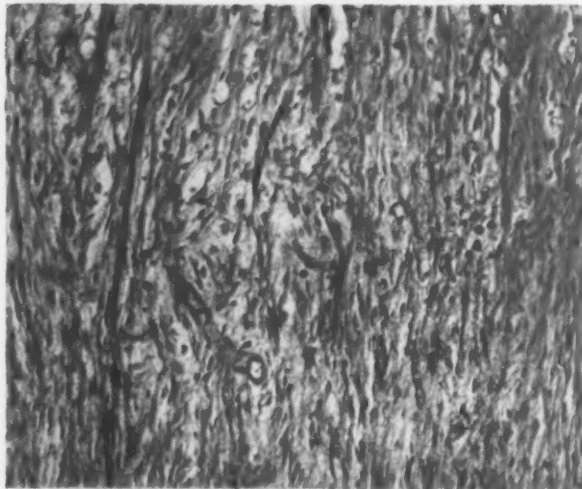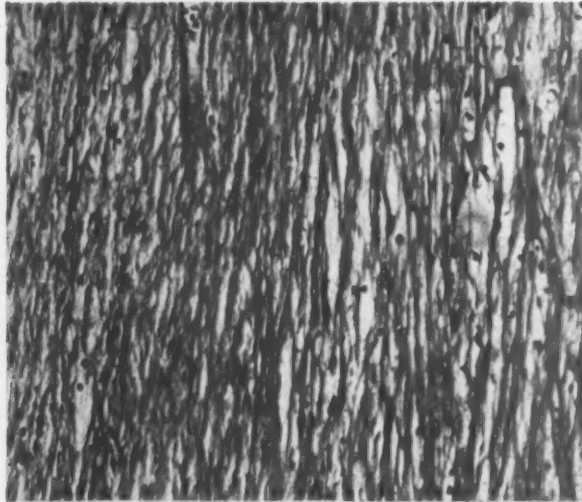


B

FIG. 5.—High power views of suture sites 14 days old. Microphotographs (A) taken from nerve in Figure 4 shows structural continuity which is not quite complete in (B) where macrophages are seen at the suture line. (Hematoxylin and eosin, x 150.)

achieve a greater tensile strength value at a certain time when their ends were accurately coapted and well-joined. It appeared that the general condition of the animal too played a rôle in governing the rate of healing at the suture site.

FIG. 6.—Nerve sutured with plasma clot and removed
18 days later. Structural continuity has been restored.
(Hematoxylin and eosin, x 27.)

TABLE I

SHOWING THE RESULTS OF TENSILE STRENGTH DETERMINATIONS OF BOTH THE INTACT SCIATIC NERVES
AND ALSO NERVES SUTURED WITH AUTOLOGOUS PLASMA CLOT IN RABBITS

Tensile Strength (in Gm.) of

| Rabbit No. | Sutured Nerve | | | Intact Nerve | | | Age of Sutured Nerve (in Days) |
|---|---|---|---|---|---|---|---|
| | Right | Left | Average | Right | Left | Average | |
| 1......... | 30 | 30 | 30 | 820 | 820 | 820 | 6 |
| 2......... | 317 | 395 | 356 | 600 | 817 | 708 | 10 |
| 3......... | 875 | 900 | 888 | 900 | 977 | 939 | 13 |
| 4......... | 1,100 | 900 | 1,000 | 800 | 1,277 | 1,038 | 13 |
| 5......... | 500 | 900 | 700 | 1,177 | 1,300 | 1,238 | 17 |
| | Poor apposition at suture site | | | | | | |
| 6......... | 600 | 617 | 609 | 651 | 600 | 626 | 19 |
| 7......... | 1,350 | 1,250 | 1,300 | 1,350 | 1,250 | 1,300 | 21 |
| 8......... | 800 | 827 | 814 | 827 | 850 | 838 | 24 |
| 9......... | 1,327 | 1,627 | 1,477 | 1,427 | 1,527 | 1,477 | 24 |
| 10......... | 1,227 | 1,667 | 1,447 | 1,007 | 1,227 | 1,117 | 28 |
| 11......... | 1,227 | 1,200 | 1,214 | 1,227 | 1,300 | 1,264 | 28 |
| 12......... | 800 | 600 | 700 | 1,527 | 1,327 | 1,427 | 36 |
| | Poor apposition at suture site | | | | | | |
| 13......... | With load of over 1,200 Gm. nerve broke at point of application of clamp rather than at suture site | | | 1,227 | 1,200 | 1,214 | 48 |
| 14......... | With load of over 1,550 Gm. nerve broke at point of application of clamp rather than at suture site | | | 1,600 | 1,550 | 1,575 | 65 |

Rupture of the nerve following the application of a weight-load which was greater than it could hold, occurred at the suture line or, in a few instances, along the point of application of the clamp. At the suture site there was a fusiform enlargement amounting to 1–2 mm. In those cases where the strength of the sutured nerve equaled that of the intact nerve the stretch occurred to a greater extent along the nerve segment than at the suture site. The strength of the silk tension sutures removed at different intervals after operation showed considerable variation. After the age of 13 days they usually broke with the small weight-load of but a few Gm.



A                                                          B
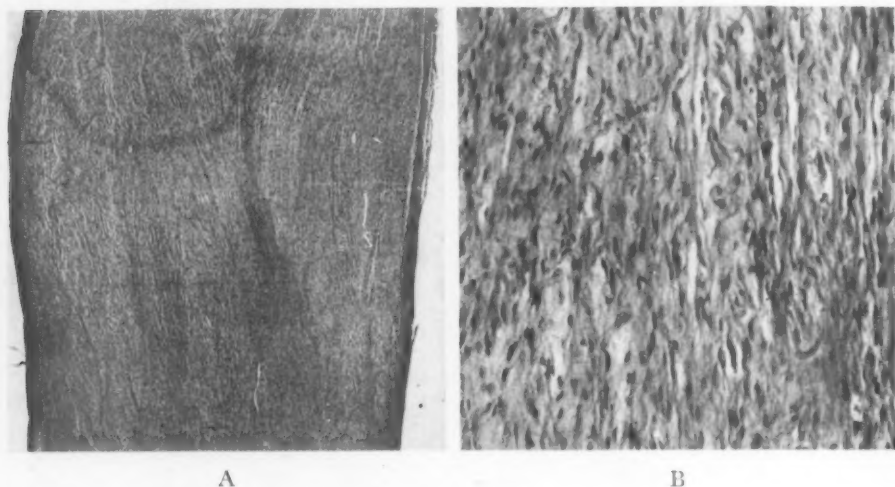
FIG. 7.—Nerve sutured with plasma clot and removed 30 days later. Complete restoration of structural continuity has occurred, including the regrowth of axis cylinders through the suture line. The suture line is free from inflammatory or fibroblastic reaction. (Hematoxylin and eosin, (A) x 21; (B) x 150.) All photographs are from sections taken from dogs' sciatic nerves which were sutured with autologous plasma clot.

DISCUSSION.—The results of tensile strength determinations indicate that the rabbits' sciatic nerve of varying sizes sutured with plasma clot achieves the tensile strength of the intact nerve within a period of three weeks. That this statement holds also for nerves sutured with silk is rather suggested by the investigations of Miller.[4] Our microscopic observations in dogs indicate that this statement applied also to this species since structural continuity at the suture line was found to be complete at approximately this time. There is no reason to suppose that there might be any appreciable difference in the healing time of sutured nerves in man. It seems justifiable then to advocate the removal of plaster of paris encasements or other means of limb fixation three weeks after nerve suture and the institution of gradual extension of the joint at this time. These experiments indicate that there would be no danger of rupture of the suture site in well-made unions when a nerve is subjected to any strain three weeks after suturing. However, there is no doubt that there

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is a limit to which a nerve may be stretched and yet remain capable of regenerating, with resultant functional recovery of the innervated part. Highet and Sanders[9] performed extensive resections of the external popliteal nerve of the dog, suturing the nerve with the knee acutely flexed. Subsequent extension of the limb after a period of 14 days resulted in considerable histologic change apart from rupture of the suture site in some instances. The increase in length of the nerve following extension of the joint resulted from elongation of it, whereas the straightening out of the tortuosity of the nerve played only a minor part. Rapid stretching in their animals did not produce any more damage than a more gradual stretching. The animal experiments of Denny-Brown and Doherty[10] demonstrated, likewise, that great damage to nerves accompanies transient stretches applied to them. Highet and Holmes[11] recorded cases in which lateral popliteal nerves were sutured with knees acutely flexed. The limit of stretch had apparently been exceeded in these patients since no recovery followed extension of the limb and microscopic examination of the nerves showed that they had been converted to fibrous tissue. It is a matter of common surgical experience, however, that nerves may be sutured with joints moderately flexed and good functional recovery result. However, the exact limit of nerve stretch that is compatible with satisfactory return of function can not at present be stated. Information is sorely needed on the results of nerve grafting and nerve stretching which are the only present alternatives to nerve suture with joints acutely flexed. Such data, together with information on the functional results following closure of gaps of varying sizes by end-to-end suture of nerves with joints flexed at different angles and then extended, is necessary in order to enable the surgeon to decide which procedure is likely to result in better recovery. The results of nerve grafting have thus far been disappointing, but with the use of the plasma clot technic for forming and suturing cable autografts[12] this method of grafting may yet prove of value.

## SUMMARY

In a series of rabbits and dogs the sciatic nerves were cut and sutured with plasma clot and the nerves were removed at various intervals after operation. Combined microscopic observations and tensile strength determinations of the sutured nerves indicated that the tensile strength value of the intact nerve is regained approximately three weeks after operation and structural continuity at the suture line is restored at this time. It is concluded that in those cases in which joints must be flexed in order to perform end-to-end suture of nerves and the extremity encased in plaster, the encasement may be removed three weeks later without danger of rupture of the suture site during the subsequent extension of the limb.

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# BRIEF COMMUNICATION

## ENEMA TUBE PERFORATION OF THE COLON

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There are many reports in the literature of perforations of the colon, some the result of the use of various types of enema tubes, others from the injection of fluids and air, and still others from the introduction of foreign objects. Fortunately, perforation of the colon by an enema tube or catheter, used in irrigation of a colostomy, is exceedingly rare.

Of the three cases reported, two of the patients sustained perforations of the colon at home. In the third case, perforation occurred while the patient was still in the hospital. The three patients had a terminal colostomy in the left lower quadrant of the abdomen subsequent to removal of the rectum for carcinoma.

It is common practice to irrigate the colon through a colostomy in the postoperative management of combined abdomino-perineal resections. In the vast majority of cases irrigations are accomplished without accidents, but, on rare occasions, undue force may carry the tube through the bowel. It has been suggested, however, that in some cases where there is a short mesocolon, an angulation of the bowel is formed, with the result that it is extremely difficult to get the catheter beyond the point of angulation. Repeated pressure of the enema tube against the angulation may result in pressure necrosis and perforation.

The clinical course is a rapid onset of pain, following the escape of the enema into the abdomen, with a rapidly developing peritonitis. Two of these patients were operated upon the day of perforation because of typical onset of symptoms. The third patient was not operated upon until three weeks following perforation. The enema apparently was placed into a walled-off pocket which prevented the escape of colon contents into the general abdominal cavity. All of the patients lived, and eventually were discharged from the hospital.

### CASE REPORTS

Case 1.—O. S., male, age 77. This patient had a combined abdomino-perineal resection one year previously. He reëntered the hospital because of abdominal pain of six hours duration, as the result of an enema administered into the colostomy. Examination revealed a surgical abdomen. Exploration demonstrated a small perforation in the medial side of the colon. The patient's postoperative course was uneventful. He was discharged on the 14th day.

Case 2.—C. C., male, age 53. Six weeks after a combined abdomino-perineal resection the patient was readmitted to the hospital with what seemed to be a generalized peritonitis following an enema administered through the colostomy. At operation, a small perforation on the medial side of the sigmoid colon was found. Later, a large abscess in
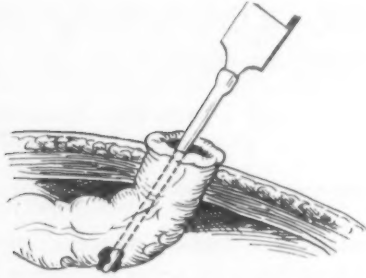
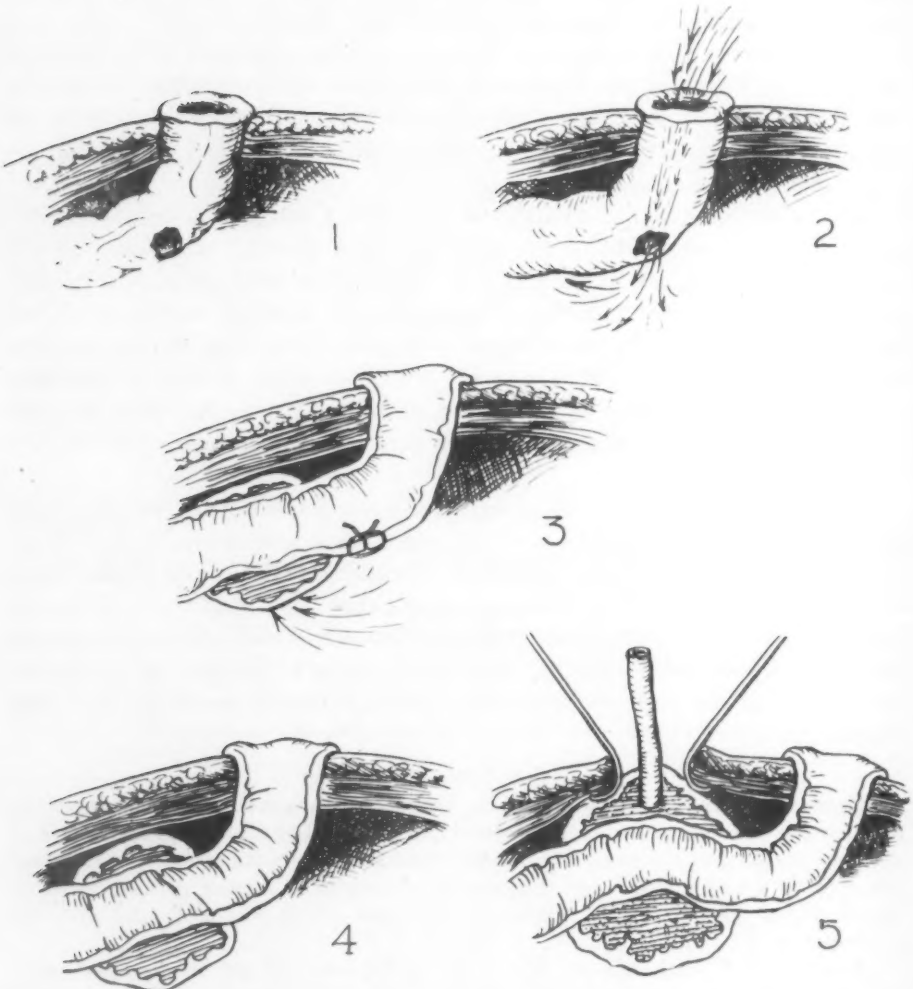FIG. 1.—Case 1: Location of perforation in sigmoid colon.



FIG. 2.—Case 2: Secondary abscess subsequent to suture of perforation.

the region of the colostomy was drained. Following this secondary drainage convalescence was uneventful.

**Case 3.**—F. Z., female, married, age 58. Two days after a combined abdomino-perineal resection an enema was administered through the colostomy, without any immediate abdominal distress. On the 4th postoperative day marked abdominal distention developed, associated with signs of a localized peritonitis. Decompression of the abdomen with a Miller-Abbott tube was carried out. Three weeks later an abscess was drained. Prompt recovery followed.

In the postoperative care of colostomies, Dr. Vernon C. David has used a technic that avoids the danger of perforation. This method suggests the use of a catheter which is placed through an inverted rubber nipple, similar to the type used on a baby's bottle. The nipple, with the catheter, is placed in the colostomy. This provides a water-tight compartment, so that when the enema fluid is injected the bowel lumen becomes distended. In this way the
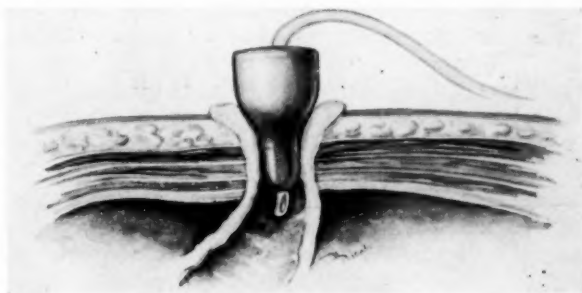


FIG. 3.—A safe procedure for irrigation of a colostomy, as recommended by Doctor David.

catheter does not readily strike the wall of the intestine, and avoids pressure necrosis and perforation.

The lesson learned in these cases is the recognition of the danger from the use of an enema tube or catheter, whether it be in skilled or unskilled hands. Before a patient is permitted to give himself an enema he should be instructed carefully in the method of introducing the catheter into the colon. The practice of carrying the catheter any distance into the colon should be forbidden. A simple insertion of the tube into the colostomy should never be farther than the depth of the abdominal wall. This procedure is certainly the safest technic.

Many patients may use an enema tube through a colostomy for years without injury to the colon. However, we feel the rarity of the complication should not permit laxity on the part of anyone in the management of these cases. Residents, interns, and nurses should be cautioned concerning the danger of perforation in the postoperative management of colostomies.

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# BOOK REVIEW

### Diagnosis and Treatment of Menstrual Disorders and Sterility

By Charles Mazer, M.D., and S. Leon Israel, M.D. 570 pages and 107 illustrations. Paul B. Hoeber, Inc., N. Y.

Menstrual disorders are among the most distressing conditions from which women suffer, and with which the physician must contend. When such dysfunction is associated with sterility in the married women it is one of the main causes of marital unhappiness.

To explain the reasons for physiologic dysfunction in the female and the causes which lead to sterility, Mazer and Israel succinctly describe in this volume the factors which play important rôles in the etiology and treatment of menstrual disorders and sterility. The normal physiologic menstrual functioning of the female depends upon the harmonious action of the pituitary, ovary and uterus. In order that the clinician and student may more readily appreciate the abnormal conditions from which women suffer, these authors appropriately preface their publication with a review of the anatomy and physiology of these organs.

A feature of each section is the authors' advice as to the therapeutic measures which, in their hands, have proved valuable. They present an evaluation of the medicaments usually used in clinical practice based upon their own experience or upon authoritative reports.

The section on amenorrhea is thoroughly and painstakingly well done. In the treatment of idiopathic amenorrhea and sterility, irradiation plays an important rôle and the authors substantiate its position as the correct mode of therapy, though they acknowledge, as do others, that "the *modus operandi* of low dosage irradiation of the pituitary gland and ovaries in restoring their functional activity and the menstrual rhythm is as yet obscure." But that irradiation does produce effective results is amply supported by their carefully supervised clinical experience. They too, note that irradiation when properly applied is harmless to both the mother and to the children born following such therapy. They appropriately call attention to the necessary caution, "one must, nevertheless, remember that in ovarian irradiation the margin between the harmless and the harmful dose is limited, and variation in dosage should for the present be definitely avoided. Therefore, only the skilled roentgenologist should be entrusted with this treatment."

Irradiation plays an important part in the treatment of uterine dysfunctions and in the treatment of fibroids, although this mode of therapy is not mentioned by the authors in the chapter on uterine fibroids.

This reviewer is not in accord with the authors' opinion regarding the treatment of menorrhagia with irradiation. In his hands irradiation has proved satisfactory in most instances.

More and more clinicians have come to realize that it is not always the female who is to blame for the barren marriage and that it is equally important to examine the husband for infertility. The section on male sterility by Dr. Charles W. Charny is excellent.

The appendix, listing in detail the commercial endocrine products available to the clinician, and the authors' evaluation of their worth, is an added aid to the doctor who treats menstrual disorders.

The book is well-printed and illustrated; the paper, exceptionally good. The authors' style makes pleasurable reading. All in all, it is a good book.

Ira I. Kaplan, M.D.